

Research Article

Mortality in Hospitalized Children Aged 1-59 Months with Pneumonia at Two Tertiary Hospitals in Harare, Zimbabwe

Makanda-Charambira PD^{1*}, Mujuru HA¹, Ndhlovu A², Timire C³, and Nathoo KJ¹

¹Department of Medicine and Health Sciences, University of Zimbabwe, Zimbabwe.

²Baines Imaging Group Harare, Zimbabwe

³Ministry of Health and Child Care National TB control program, Harare, Zimbabwe

***Corresponding author**

Makanda-Charambira PD, Child And Adolescent Health Unit, Faculty of Medicine and Health Sciences, University of Zimbabwe P.O. Box A178, Avondale, Harare, Zimbabwe Tel: 263242 2791631, Email: pmakanda@psmi.co.zw

Submitted: 24 December 2020

Accepted: 21 January 2021

Published: 23 January 2021

ISSN: 2373-9312

Copyright

© 2021 Makanda-Charambira PD, et al.

OPEN ACCESS**Keywords**

- Pneumonia
- Mortality
- Hypoxia
- Infection

Abstract

Background: Pneumonia is among the leading causes of mortality in children, accounting for 13% of global under 5 mortality. Studies to determine factors contributing to mortality in childhood pneumonia can help optimize utilization of scarce resources for the most effective preventive and early management strategies in resource limited settings.

Methods: This hospital based analytical cross-sectional study was conducted between 1 April and 30 July 2017. Hospitalized children aged 1 month to 59 months with WHO defined pneumonia/severe pneumonia were enrolled. They were evaluated to ascertain demographic characteristics, clinical features and laboratory features within 24 hours of admission as related to hospital stay and mortality.

Results: A total of 309 children were enrolled. The median age was 3 months (IQR 2-10 months) with those aged 2-11 months constituting 61.1% (n=189). Hypoxia was noted in 210 (68.0%) children and clinical features associated with hypoxia on admission were chest wall in drawing (p<0.001), grunting (p <0.001) and lethargy (p <0.001). Median hospital stay was 5 days (IQR: 3-8). The median hospital stay increased significantly with decreasing age (p=0.01) and children with chest X-ray abnormalities on admission were four times more likely to have a prolonged stay in hospital compared to children with normal chest X-rays. Overall mortality rate was 14.2% (n=44) with 36% (n=15) of total deaths occurring within 24hrs of admission. Factors strongly associated with mortality were: severe pneumonia (p=0.001), lethargy (p=0.0001), HIV infection (p=0.0001), hypoxia (p=0.001), central cyanosis (p=<0.001), grunting (p=<0.001), chest wall in drawing (p=0.001) comorbidities (p=<0.0001) and severe malnutrition (p=<0.0001).

Conclusion: Pneumonia remains a major cause of mortality among hospitalized children in Zimbabwe. Presence of lethargy, hypoxia, HIV infection, comorbidities, severe malnutrition and signs of severe pneumonia such as grunting, cyanosis, head nodding and chest wall in drawing are associated with increased odds of dying.

ABBREVIATIONS

WHO: World Health Organization; UNICEF: United Nations Children's Emergency Fund; MCEE: Maternal And Child Epidemiology Estimation Group; MICS: Multi Cluster Indicator Survey; HIV: Human Immunodeficiency Virus; MTCT: Mother To Child Transmission; PMTCT: Prevention Of Mother To Child Transmission; AIDS: Acquired Immunodeficiency Syndrome; DNA PCR: DNA Polymerase Chain Reaction; PCV: Pneumococcal Conjugate Vaccine; DPT: Diphtheria Pertussis Tetanus; PJP: Pneumocystis Jirovecii Pneumonia; PCP: Pneumocystis Carinii Pneumonia; GINA: Global Initiative For Asthma; MUAC: Mid Upper Arm Circumference; Hb: Hemoglobin; DBS: Dried Blood Spot; MRCZ: Medical Research Council Of Zimbabwe; JREC: Joint Research Ethics Committee

INTRODUCTION

Pneumonia is among the leading causes of mortality in children globally and accounts for 13% of under 5 mortality [1]. It is an entirely preventable disease but kills more children than any other illness in the world [2], making it a major target to achieve the sustainable development goals 3(SDG 3), of reducing mortality. The number of children dying from pneumonia has decreased substantially over the past three decades. In 1990, more than two million children died from pneumonia; by 2017 this number had fallen to 809,000 globally [3]. Most of these deaths occurred in Sub Saharan Africa and South Asia. In 2017, 245 per 100 000 children under 5 years died from pneumonia in Zimbabwe [1].

Factors contributing to mortality from childhood pneumonia include young age [14], HIV infection [4,15], prematurity [5],

malnutrition [6], and disease severity at presentation [7]. HIV infection is associated with increased mortality from pneumonia, infected children being at higher risk than unexposed or exposed but uninfected children [4,15]. HIV exposed uninfected children have a general greater risk of hospitalization in their first year of life compared to HIV unexposed children [12]. Antiretroviral therapy, however significantly reduces mortality from severe pneumonia [13].

Decline in mortality has been attributed to increased availability of vaccines and antibiotics as well as improvements in the major risk factors such as malnutrition, high air pollution and poor sanitation [3]. Immunization against *S. pneumoniae*, *H. influenzae type b* and measles virus reduce the prevalence and mortality from pneumonia [8-11].

Since the last study in Zimbabwe on mortality from pneumonia in 1989, many programmatic interventions directly impacting pneumonia in children have been implemented in the health sector including introduction of *H. influenzae* and pneumococcal vaccines, roll out of prevention of mother to child transmission of HIV and improved access to anti-retroviral therapy. The aim of this study was to describe the clinical characteristics and factors associated with mortality in children aged 1-59 months admitted to tertiary hospitals in Harare.

MATERIALS AND METHODS

The study was conducted in the pediatric medical wards of two tertiary hospitals in Harare, the capital city of Zimbabwe. Children aged between 1 and 59 months hospitalized with WHO defined pneumonia/severe pneumonia were enrolled. Children diagnosed with asthma based on the Global Initiative of Asthma (GINA) definition [16], and inter hospital transfer patients were excluded. Convenient sampling was done and only children admitted from Monday to Friday were enrolled into the study.

Patients were assessed in the emergency department by the attending doctor and managed according to the local treatment guidelines. Enrollment into the study was within 24 hours of admission. Demographic data, including maternal /caregiver characteristics were recorded. A complete clinical examination was done and details of the respiratory distress, nutritional status, and any signs of shock [17], were captured. Oxygen saturations were monitored by pulse oximetry throughout the admission as part of standard of care but only the oxygen saturation at baseline and discharge were recorded for the study. Dr Trust® finger pulse oximeter was used. Weight was measured using a Salter scale to the nearest 0.1kg. Length or height in children below or above 24months respectively was done using a stadiometer (UNICEF S0114540 Baby/infant/adult L-hgt measuring system/SET-2). Non dominant arm mid upper arm circumference (MUAC) was measured in all children above 6 months of age per WHO recommendations [17].

Mothers had a rapid HIV test performed on admission if there was no documented HIV test result done within the past 3 months as per to national guidelines. An appropriate HIV test was subsequently performed in the HIV exposed children. HIV exposed infants below 9 months of age had HIV DNA PCR performed if they did not have documented results performed within the previous 3 months according to national PMTCT

program guidelines. HIV exposed infants between 9-18 months had a rapid HIV test done first and positive tests were confirmed with a HIV DNA PCR test. Children above 18 months or those who had stopped breastfeeding for > 6 weeks had rapid HIV antibody test as the diagnostic test. Chest x-rays were done at the discretion of the managing team and interpreted by a certified radiologist. Days of hospital stay were recorded on discharge with duration of >5days defined as prolonged hospital stay [5].

Data were captured using EpiData software versions 3.1 for entry and version 2.2.2.182 for analysis (EpiData Association, Odense, Denmark). Data cleaning was done to check for completeness and any inconsistencies. Continuous variables were summarized using means and standard deviation or medians and inter-quartile ranges as appropriate. Categorical data were summarized using proportions. Categorical variables were compared using chi-square test as measures of effect and presented as odds ratios with 95% confidence intervals. Level of significance was set at 5%.

Permission to conduct the study was obtained from Harare Central Hospital Ethics Committee (HCEC 150217/ 07), Joint Research Ethics Committee (JREC) for the University of Zimbabwe Faculty of Medicine and Health Sciences (JREC/61/17) and the Medical Research Council of Zimbabwe.

RESULTS

A total of 568 children aged below 59 months were admitted with the diagnosis of pneumonia/severe pneumonia at the 2 tertiary hospitals during the study period 1st April to 30th July 2017. Of these 523(92.1%) were aged between 1 - 59 months and therefore eligible for the study. A total of 309 children were enrolled into the study, with 210 (68.0%) and 99 (32.0%) having severe pneumonia and pneumonia respectively based on WHO definitions.

The median age was 3 months (IQR; 2-10months) with males (59.5%) and children aged 2-11 months constituting the majority (Table 1). Of the 196 children below 6 months of age, 107 (54.6%), were on exclusive breastfeeding and 254 (87.6%), of all children aged less than 24 months were still being breastfed. Three hundred and eight children (99.7%), were tested for HIV or had a recorded HIV result. Of these, nineteen (6.1%), children were confirmed to be HIV infected and 33 (10.7%), were exposed but uninfected (HEU), while the rest were unexposed. Only 6 (31.6%), of the 19 HIV infected children and 25 (75.6%), of the 33 HEU were on cotrimoxazole prophylaxis (Table 1). Immunization was incomplete for age in 63 (20.4%), children. Of these, 37 (58.7%), had missed one dose of PCV, 4 (6.3%), missed two doses and 3 (4.7%), missed all 3 doses. Under nutrition was found in 93 (30.1%), children with 55(59.1%), of them being severely malnourished. Co-morbid conditions recorded were meningitis (n=9), trisomy 21 (n=9), and cardiac disease (n=19). Diarrhea was present in 58 (18.8%) children (Table 2).

Signs of respiratory distress present on admission were grunting (n=169, 54.7%), lethargy (n=172, 55.7%), head nodding (n=127, 41.1%), and chest wall indrawing (n=141, 45.6%) (Table 3). Mean oxygen saturation on admission was of 83.19% (range 42% to 99%). Hypoxia, defined as saturation below 90% was noted in 210 (68.0%), children. There were eight children who

Table 1: Demographic characteristics of children aged 1-59 months hospitalized with pneumonia/severe pneumonia at two tertiary hospitals in Harare, Zimbabwe.

Child demographics	Total	Deceased	Alive	OR 95% CI	p-value
Age in months	n=309	n=44	n=265		
<2	53	2 (3.8)	51 (96.2)	0.18 (0.02-0.88)	0.02
11-Feb	189	30 (15.9)	159 (84.1)	0.86 (0.40-1.99)	0.7
Dec-59	67	12 (17.9)	55 (82.3)	Reference	
Gestational age at birth					
Pre-term (<37 weeks)	20	1 (5.0)	19 (95.0)	0.32 (0.01-2.20)	0.49
Term (37 weeks+)	222	31 (14.0)	191 (86.0)	Reference	
Birth weight					
<2500g	53	10 (18.9)	43 (81.1)	1.53(0.62-3.43)	0.28
≥ 2500g	250	33 (13.2)	217 (86.8)	Reference	
Area of residence					
Urban	273	35(12.8)	238(87.2)	0.44(0.19-1.02)	0.05
Rural	36	9(25.0)	27(75.0)	Reference	
Mother's age in years					
<19	12	2(16.7)	10(83.3)	Reference	0.84
≥19	292	42(14.4)	250(85.6)	0.84(0.18-3.97)	
Mothers level of education					
Secondary and above	263	35(13.3)	228(86.7)	0.53(0.24-1.21)	0.13
Primary and below	41	9(22.0)	32(78.0)	Reference	

Table 2: Presenting history of children hospitalized with pneumonia.

Child history	Total	Deceased	Alive	OR 95% CI	p value
Cough duration					
≥14 days	30	3 (11.1)	27(88.9)	0.79(0.15-2.81)	1
<14days	260	32 (12.3)	228 (87.7)	Reference	
Comorbidities					
Yes	37	13 (35.1)	24 (64.9)	4.21(1.95-9.11)	<0.0001
No	272	31 (11.4)	241 (88.6)	Reference	
Diarrhoea					
Yes	58	12(20.7)	46(79.3)	1.79(0.86-3.73)	0.12
No	251	32(12.7)	219(87.3)	Reference	
Previous admission (pneumonia)					
Yes	49	5 (10.2)	44 (89.8)	0.64(0.24-1.73)	0.38
No	260	39 (15.0)	221 (85.0)	Reference	
< 6mo exclusive breastfeeding					
No	89	13 (14.6)	76 (85.4)	1.66(0.69-3.99)	0.25
Yes	107	10 (9.3)	97 (90.7)	Reference	
<24mo still breastfeeding					
No	36	10(27.8)	26(72.2)	2.58(1.14-2.82)	0.02
Yes	254	33(13.0)	221(87.0)	Reference	
HIV status					
HIV-infected	19	8 (42.1)	11 (57.9)	5.92(2.20-15.96)	0.0001
HIV-exposed uninfected	33	8 (24.2)	25 (75.8)	2.61(1.07-6.33)	0.03
HIV unexposed	256	28 (10.9)	228 (89.1)	Reference	

Cotrimoxazole given					
No	21	5 (23.8)	16 (76.2)	0.58(0.17-2.01)	0.39
Yes	31	10 (32.3)	21 (67.7)	Reference	
Pre-referral antibiotics					
Yes	140	15(10.7)	125(89.3)	0.58(0.30-1.13)	0.11
No	169	29(17.2)	140(82.8)	Reference	
Immunization status					
Not up to date	63	12(19.0)	51(81.0)	1.57(0.76-3.27)	0.22
Up to date	246	32(13.0)	214(87.0)	Reference	

were critically ill on admission with unrecordable saturations due to shock. Clinical features associated with hypoxia on admission were chest wall indrawing ($p < 0.0001$), grunting ($p < 0.0001$), and lethargy ($p < 0.0001$), on univariate analysis. All these remained significant on multivariate analysis (Table 2). Fever and malnutrition were not associated with hypoxia on admission. Chest X-rays were performed in 119 (38.5%) children. Normal chest x-ray findings were reported in 30 (25.2%) children while other x-ray findings were unilobar infiltrates in 24 (20.2%), multilobe infiltrates in 59 (49.6%), pleural effusions in 6 (5.0%) children. No association was found between an abnormal chest X-ray and mortality (OR 3.07; CI 0.66-14.2).

The mean saturation on discharge was 93.75% (SD 3.69). A total of 23 (8.7%) children had saturation below 90% at discharge and the lowest was 78%. One patient did not have oxygen saturation measured at discharge.

Median hospital stay was 5 days (IQR: 3-8). Children admitted with chest wall indrawing and those with lethargy were about twice more likely to be admitted for more than five days compared to those without these clinical signs (Table 5). The median hospital stay increased significantly with decreasing age ($p = 0.01$). The median hospital stay decreased from 6 days (IQR: 4 - 7) among children aged under 3 months to 3.5 days (IQR: 2.0 - 6.3) among children above 3 months. Children with chest X-ray abnormalities on admission were four times more likely to have a prolonged stay in hospital when compared to children with a normal chest X-ray (Table 5).

The case fatality rate was 14.2% ($n = 44$), with 36% ($n = 16$), of total deaths occurring within 24hrs of admission. The rate was highest in the 12 to 59 months age group (17.9%), compared to 2 to 11 (15.9), and those 1-2 months (3.8%) (Table 1). Age between 1 and 2 months, lethargy, HIV infection, hypoxia, central cyanosis, grunting, severe malnutrition and comorbidities were significantly associated with mortality. Gender, fever, history of prematurity, birth weight and concurrent diarrhea were not associated with mortality

Children diagnosed with severe pneumonia had 8.6 times the odds of dying compared to those with pneumonia ($p = 0.001$), and those who presented with lethargy had almost 22 times the odds of dying compared to those without ($p < 0.0001$). Children with central cyanosis on admission were 3.34 times likely to die ($p < 0.001$) (Table 6). HIV infected children admitted with pneumonia were almost six times more likely to die compared to HIV unexposed uninfected ($p = 0.0001$). The odds of dying among

children that were severely malnourished was about five times that of children who were well nourished ($p < 0.0001$).

There was no association between exclusive breastfeeding and mortality in infants below 6 months ($p = 0.25$). However, children below 24 months who were no longer being breastfed had twice the odds of dying compared to those who were still being breastfed ($p = 0.02$).

Presence of leukocytosis or leukopenia increased the risk of mortality 3 and 5 times respectively compared to normal white cell count in these children, while the risk was about six times if urea levels were high ($p < 0.0001$) and 4 times if there was thrombocytopenia ($p = 0.01$). Abnormal serum sodium levels also increased risk of mortality (Table 7).

DISCUSSION

Pneumonia remains a major cause of mortality in hospitalized children with a case fatality rate of 14.2 % in this study and an unacceptably high proportion dying within 24hrs. This was similar to the 15% case fatality rate documented almost 30 years ago by Nathoo et al in Zimbabwean under 5 children with pneumonia [4]. The finding of higher mortality in male children is in agreement with other studies conducted in Africa and other parts of the world [19,45,46].

The reported strong association between age less than 1 year and risk of mortality from pneumonia was not evident in this present study [4,19,20]. This could be due to possible inclusion of viral bronchiolitis by using WHO case definition of pneumonia. However the high case fatality rate in children above 12 months of age in our study could be due to the higher numbers of HIV infected and HIV exposed uninfected in this age group unlike in the previous study by Nathoo et al were most HIV infected children were under 12 months of age [4]. As in our study, HIV exposed uninfected children with pneumonia have been shown to be at increased risk of mortality compared to HIV unexposed [15,4].

Breastfeeding during the first 23 months of life has been shown to be a key intervention for reducing pneumonia morbidity and mortality [40]. In this study breastfeeding was protective in children aged less than 24 months. Numerous immunological components of breast milk protect against respiratory infections [21]. Previous studies have documented young maternal age, low maternal education as being associated with increased risk of death [22]. No maternal related factors were found to be related to mortality in our study possibly due to small sample analyzed

Table 3: Examination findings of children hospitalized with pneumonia.

Child presentation on examination	Total	Deceased	Alive	OR 95% CI	p-value
	N=309	N=44	N=265		
Grunting					
Yes	169	37 (21.9)	132 (78.1)	5.33 (2.29-12.37)	<0.001**
No	140	7 (5.0)	133 (95.0)	Reference	
Lethargy					
Yes	172	42 (24.4)	130 (75.6)	21.81 (5.17-91.9)	<0.0001
No	137	2 (1.5)	135 (98.5)	Reference	
Head nodding					
Yes	127	27 (21.3)	100 (78.7)	2.62 (1.36-5.05)	0.003**
No	182	17 (9.3)	165 (90.7)	Reference	
Chest wall indrawing					
Yes	141	31 (30.0)	110 (70.0)	2.50 (1.19-5.46)	0.001**
No	168	13 (7.7)	115 (92.3)	Reference	
Central cyanosis					
Yes	83	22 (26.5)	61 (73.5)	3.34 (1.73-6.45)	<0.001**
No	226	22 (9.3)	204 (90.3)	Reference	
Oxygen saturation at admission					
<90%	210	34 (16.2)	176 (83.8)	8.60 (2.11-75.12)	0.001**
≥90%	91	2 (2.2)	89 (97.8)	Reference	
Nutritional status					
Severe malnutrition	55	18 (32.7)	37 (62.3)	5.05 (2.36-10.81)	<0.0001**
Moderate malnutrition	38	8 (21.1)	30 (78.9)	2.77 (1.09-7.04)	0.03**
Well nourished	182	16 (8.8)	166(91.2)	Reference	
Fever					
Yes	199	29(14.6)	170(85.4)	1.08(0.55-2.12)	0.82
No	110	15(13.6)	95(86.5)	Reference	

Table 4: Factors associated with hypoxia in children hospitalized with pneumonia.

	Total	Hypoxia (%)	Crude OR	p-value	OR	p-value
Comorbidities						
Yes	36	33 (91.7)	5.47	0.002	4.14	0.03
No	265	177 (66.8)	ref	ref		
Chest wall indrawing						
Severe	138	122 (88.4)	6.5	<0.0001	3.64	<0.001
Non-severe	163	88 (54.0)	ref	ref		
Lethargy						
Yes	164	138 (84.1)	4.79	<0.0001	2.66	0.001
No	137	72 (52.6)	ref	ref		
Grunting						
Yes	161	134 (83.2)	4.18	<0.0001	2.59	0.001
No	140	76 (54.3)	ref	ref		

Malnutrition [31-34], and other comorbidities' [22,35] association with mortality in children with pneumonia are well documented Our study also supports earlier studies which identified head nodding, grunting, chest wall in drawing and cyanosis as clinical signs that predict mortality [22,23] while

chest wall in drawing, grunting and lethargy were predictors of hypoxia in children with pneumonia [24-27]. Importantly, central cyanosis is insensitive for accurate detection of hypoxia, as it identifies between 9-42% of children with hypoxemia [28,29]. WHO recommends the use of pulse oximetry in all neonates

Table 5: Factors associated with prolonged hospital stay in children hospitalized with pneumonia.

Clinical feature	Long stay	Short stay	OR 95% CI	p-value
	(>5 days)	(≤ 5 days)		
Grunting				
Yes	124 (73.4)	45 (26.6)	1.06 (0.64-1.76)	0.89
No	101 (72.1)	39(27.9)	Reference	
Chest wall indrawing				
Severe	112 (79.4)	29 (20.6)	1.88 (1.12-3.16)	0.02
Non-severe	113 (69.3)	55 (32.7)	Reference	
Head nodding				
Yes	97 (76.4)	30 (23.6)	1.36 (0.81-2.29)	0.24
No	128 (70.3)	50 (29.7)	Reference	
Lethargy				
Yes	137 (79.7)	35 (20.3)	2.18 (1.31-3.63)	0.003
No	88 (64.2)	49 (35.8)	Reference	
CXR result				
Abnormal X-ray	55 (93.2)	4 (6.8)	4.18 (1.12-15.7)	0.02
Normal CXR	23 (76.7)	7 (23.3)	Reference	

Table 6: Association between full blood count and mortality in children hospitalized with pneumonia.

	Total	Deceased	Alive	OR 95% CI	p-value
	N=275	n=39	n=218		
Haemoglobin (g/dl)					
<2mo					
Low Hb (<13.4)	11	1(0.9)	10(90.9)	3.60(0.21-62.8)	0.35
Normal Hb (13.4 – 19.8)	37	1(2.7)	36(97.3)	Reference	
2-11mo					
High Hb (>14.1)	2	0 (0) †	2 (100)	Not applicable	0.53
Low Hb (<9.4)	82	14 (17.1)	68 (82.9)	1.07 (0.48-2.42)	0.86
Normal Hb (9.4 – 14.1)	87	14 (16.1)	73 (83.9)	Reference	
12-59mo					
High Hb (>13.5)	3	0 (0)	3 (100) †	Not applicable	0.54
Low Hb (<11.3)	26	6 (23.1)	20 (76.9)	2.40 (0.53-10.8)	0.25
Normal Hb (11.3 – 13.5)	27	3 (11.1)	24 (88.9)	Reference	
White cell count (X 10⁹ cells/l)					
Leucocytosis (wcc ≥18.0)					
	69	17 (24.6)	52 (75.4)	3.06 (1.49-6.32)	0.002
Leucopenia (wcc <6.0)					
	11	4 (36.4)	7 (63.6)	5.35 (1.44-19.97)	0.01
Normal (5.0-17.9)					
	197	19 (9.6)	178 (90.4)	Reference	
Platelet count (x 10⁹ /l)					
Thrombocytosis (plt>451)					
	150	16 (10.7)	134 (89.3)	0.66 (0.32-1.37)	0.26
Thrombocytopenia (<150)					
	14	6 (42.9)	8 (57.1)	4.15 (1.28-13.47)	0.01
Normal (150-450)					
	111	17 (15.3)	94 (84.7)	Reference	

Hb-hemoglobin, wcc-white cell count, plt- platelets,

and children with emergency or priority signs during triaging even at first level health centers [28], but these are usually not available. In our study 8.7% of those who had oxygen saturation measurement on discharge were hypoxic. Hypoxia on discharge has been associated with increased risk of death and readmission [30].

Electrolyte abnormalities such as hyponatremia have been

associated with increased risk of mortality in children with pneumonia [36]. In our study both high and low sodium levels at admission were associated with almost 5 times risk of dying from pneumonia. The justification for routinely measuring electrolytes in children with pneumonia in low resource setting needs to be explored.

Although in our study anaemia did not emerge as a significant risk factor for mortality, other studies have reported otherwise

Table 7: Association between urea and electrolyte levels and mortality in children hospitalized with pneumonia.

	Total	Deceased	Alive	OR 95% CI	p-value
	n=261	n= 37	n=224		
Sodium					
High (≥146 mmol/l)	32	10 (31.2)	22 (68.8)	5.80 (2.27-14.81)	0.0001
Low (113-134mmol/l)	50	14 (28.0)	36 (72.0)	4.97 (2.15-11.5)	0.0001
normal (135-145mmol/l)	179	13 (7.3)	166 (92.7)	Reference	
Urea	267	39	228		
High (≥6.5 mmo/l)	34	14 (41.2)	20 (58.8)	6.13 (2.70-13.9)	<0.0001
Low (<6.5mmol/l)	28	4 (14.3)	24 (85.7)	1.46 (0.46-4.62)	0.51
Normal (1.8-6.4 mmol/l)	205	21 (10.2)	184 (89.8)	Reference	
Creatinine	263*	39	224		
Abnormal	46	4 (8.7)	42 (91.3)	0.50 (0.12-1.50)	0.26
Normal (18-150µmol/l)	217	35 (10.8)	182 (89.2)	Reference	

[37,38]. This could be due to the small sample size of children with severe anaemia (Hb < 6g/dl) which increases mortality risk [39]. Our study also showed that abnormal leucocyte count (either high or low) is associated with increased risk of death. High leukocyte count is an indicator of severity of illness and therefore, may be associated with mortality [5]. Bone marrow function might be depressed in severe infections leading to leukopenia [40]. Platelets have an important role in antimicrobial host defenses [41]. Thrombocytopenia may develop due to severe infection, inflammation or depletion of coagulation factors and thus serves as an indicator of severity of the illness [41], and an outcome predictor in patients with severe community-acquired pneumonia. Consistent with previous studies, thrombocytopenia was associated with higher mortality in children with pneumonia [42-44].

LIMITATIONS

The study was conducted midweek which missed children who came over the weekend which might cause some bias. Although seasonal variation in pneumonia was missed since the study was not conducted over a whole year it sets precedence of future broader studies. Patients not examined soon after admission but rather within the first 24 hours of admission could have had a change in the clinical symptoms and signs after starting antibiotics and receiving oxygen therapy, however all efforts were made to examine patients in the shortest time soon after admission. ART use was not analyzed in children who were HIV infected. The degree to which anaemia contributed to the hypoxia was also not analyzed in this study. Hydration status was assessed and managed by the attending doctor but that information was not captured.

CONCLUSION

Case fatality among hospitalized children between 1 – 59 months with pneumonia remains unacceptably high. Presence of lethargy, hypoxia, HIV infection, comorbidities, severe malnutrition and signs of severe pneumonia such as grunting, cyanosis, head nodding and chest wall indrawing are associated with increased likelihood of dying. Children who are HIV exposed but uninfected have a higher likelihood of dying when compared

to those who are not HIV exposed. Strategies aimed at preventing HIV infection in children should be strengthened as presence of HIV infection increased the likelihood of mortality.

Breastfeeding up to 2 years of age was associated with a reduced risk of mortality in children with pneumonia. Low-cost high impact initiatives like breastfeeding up to 2 years of age should continue being encouraged.

Children with pneumonia who have chest wall indrawing, grunting, lethargy and presence of comorbidities were likely to have low oxygen saturations. Pulse oximetry should be made available in the emergency department to allow measurement of oxygen saturation on admission since cyanosis is not sensitive in identifying children with hypoxia. Oxygen saturation should be measured on discharge to avoid discharge of hypoxic children at risk of later mortality.

ACKNOWLEDGEMENTS

The authors are grateful to Kelvin Charambira for assisting with statistical analysis, parents/caregivers and children who participated in the study.

REFERENCES

- Roser M, Ritchie H, Dadonaite B. Child and Infant Mortality. Our World in Data. 2013; 10: 18
- dpicampaigns. 'Forgotten' pneumonia epidemic kills more children than any other disease. United Nations Sustainable Development. 2020.
- Pneumonia — no child should die from a disease we can prevent. Our World in Data. 2020.
- Nathoo KJ, Nkrumah FK, Ndlovu D, Nhembe M, Pirie DJ, Kowo H. Acute lower respiratory tract infection in hospitalized children in Zimbabwe. *Ann Trop Paediatr.* 1992; 13: 253-261.
- Tiewsoh K, Lodha R, Pandey RM, Broor S, Kalaivani M, Kabra SK. Factors determining the outcome of children hospitalized with severe pneumonia. *BMC Pediatr.* 2009; 9: 15.
- Rice AL, Sacco L, Hyder A, Black RE. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization.* 2000; 78: 1207-1221.

7. Ramachandran P, Nedunchelian K, Vengatesan A, Suresh S. Risk factors for mortality in community-acquired pneumonia among children aged 1–59 months admitted in a referral hospital. *Indian Pediatr.* 2012; 49: 889-895.
8. Bloch AB, Orenstein WA, Stetler HC, Wassilak SG, Amler RW, Bart KJ, et al. Health impact of measles vaccination in the United States. *Pediatrics.* 1985; 76: 524-532.
9. Simonsen L, Taylor RJ, Young-Xu Y, Haber M, May L, Klugman KP. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. *MBio.* 2011; 2: e00309-310.
10. Becker-Dreps S, Amaya E, Liu L, Moreno G, Rocha J, Briceño R, et al. Changes in childhood pneumonia and infant mortality rates following introduction of the 13-valent pneumococcal conjugate vaccine in Nicaragua. *Pediatr Infectious Dis Journal.* 2014; 33: 637-642.
11. Theodoratou E, Johnson S, Jhass A, Madhi SA, Clark A, Boschi-Pinto C, et al. The effect of Haemophilus influenzae type b and pneumococcal conjugate vaccines on childhood pneumonia incidence, severe morbidity and mortality. *Int J Epidemiol.* 2010; 39: i172-i185.
12. Slogrove A, Reikie B, Naidoo S, De Beer C, Ho K, Cotton M, et al. HIV-exposed uninfected infants are at increased risk for severe infections in the first year of life. *J Tropical Pediatr.* 2012; 58: 505-508.
13. The impact of antiretroviral treatment on the burden of invasive pneumococcal disease in South African children: a time series. 2016.
14. Bokade CM, Madhura AD, Bagul AS, Thakre SB. Predictors of mortality in children due to severe and very severe pneumonia. *Nigerian Med J.* 2015; 56: 287.
15. Theodoratou E, McAllister DA, Reed C, Adeloye DO, Rudan I, Muhe LM, et al. Global, regional, and national estimates of pneumonia burden in HIV-infected children in 2010: a meta-analysis and modelling study. *Lancet Infect Dis.* 2014; 14: 1250-1258.
16. Global Initiative for Asthma. *Global Strategy for Asthma Management and Prevention.* 2016.
17. WHO, UNICEF. WHO child growth standards and the identification of severe acute malnutrition in infants and children. A Joint Statement by the World Health Organization and the United Nations Children's Fund. 2009.
18. What is the mortality rate for children with bronchiolitis? 2020.
19. Sehgal V, Sethi GR, Sachdev HPS, Satyanarayana L. Predictors of mortality in subjects hospitalized with acute lower respiratory tract infections. *Indian Pediatr.* 1997; 34: 213-219.
20. Leowski J. [Mortality from acute respiratory infections in children under 5 years of age: global estimates]. *World health statistics quarterly Rapport trimestriel de statistiques sanitaires mondiales.* 1986; 39: 138-144.
21. Lamberti LM, Zakarija-Grković I, Fischer Walker CL, Theodoratou E, Nair H, Campbell H, et al. Breastfeeding for reducing the risk of pneumonia morbidity and mortality in children under two: a systematic literature review and meta-analysis. *BMC Public Health.* 2013; 13: S18.
22. Sonogo M, Pellegrin MC, Becker G, Lazzarini M. Risk factors for mortality from acute lower respiratory infections (ALRI) in children under five years of age in low and middle-income countries: a systematic review and meta-analysis of observational studies. *PLoS ONE.* 2015; 10: e0116380.
23. Shann F, Barker J, Poore P. Clinical signs that predict death in children with severe pneumonia. *Pediatr Infect Dis J.* 1989; 8: 852-855.
24. Laman M, Ripa P, Vince J, Tefuarani N. Can clinical signs predict hypoxaemia in Papua New Guinean children with moderate and severe pneumonia? *Ann Trop Paediatr.* 2005; 25: 23-27.
25. Basnet S, Adhikari RK, Gurung CK. Hypoxemia in children with pneumonia and its clinical predictors. *Indian J Pediatr.* 2006; 73: 777-781.
26. Dyke T, Lewis D, Heegaard W, Manary M, Flew S, Rudeen K. Predicting Hypoxia in Children with Acute Lower Respiratory Infection: a Study in the Highlands of Papua New Guinea. *J Trop Pediatr.* 1995; 41: 196-201.
27. Usen S, Weber M, Mulholland K, Jaffar S, Oparaugo A, Omosigho C, et al. Clinical predictors of hypoxaemia in Gambian children with acute lower respiratory tract infection: prospective cohort study. *BMJ.* 1999; 318: 86-91.
28. WHO | Oxygen therapy for children: a manual for health workers [Internet]. WHO. World Health Organization. 2020.
29. Ayieko P, English M. In Children Aged 2–59 months with Pneumonia, Which Clinical Signs Best Predict Hypoxaemia? *J Trop Pediatr.* 2006; 52: 307-310.
30. Instability on Hospital Discharge and the Risk of Adverse Outcomes in Patients With Pneumonia | Infectious Diseases | JAMA Internal Medicine | JAMA Network. 2020.
31. Lazzarini M, Seward N, Lufesi N, Banda R, Sinyeka S, Masache G, et al. Mortality and its risk factors in Malawian children admitted to hospital with clinical pneumonia, 2001–12: a retrospective observational study. *The Lancet Global Health.* 2016; 4: e57-68.
32. Rice AL, Sacco L, Hyder A, Black RE. Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bulletin of the World Health Organization.* 2000; 78: 1207-1221.
33. Suwanjutha S, Ruangkanhasetr S, Chantarojanasiri T, Hotrakitya S. Risk factors associated with morbidity and mortality of pneumonia in Thai children under 5 years. *Southeast Asian J Tropical Med Public Health.* 1994; 25: 60-66.
34. Chisti MJ, Tebruegge M, La Vincente S, Graham SM, Duke T. Pneumonia in severely malnourished children in developing countries—mortality risk, aetiology and validity of WHO clinical signs: a systematic review. *Trop Med Int Health.* 2009; 14: 1173-1189.
35. Nascimento-Carvalho CMC, Rocha H, Santos-Jesus R, Benguigui Y. Childhood pneumonia: clinical aspects associated with hospitalization or death. *Brazilian J Infectious Dis.* 2002; 6: 22-28.
36. Singhi S, Dhawan A. Frequency and significance of electrolyte abnormalities in pneumonia. *Indian Pediatr.* 1992; 29: 735-740.
37. Zhang Q, Guo Z, Bai Z, MacDonald NE. A 4 year prospective study to determine risk factors for severe community acquired pneumonia in children in southern China. *Pediatr Pulmonol.* 2013; 48: 390-397.
38. Banajeh SM, al-Sunbali NN, al-Sanahani SH. Clinical characteristics and outcome of children aged under 5 years hospitalized with severe pneumonia in Yemen. *Ann Trop Paediatr.* 1997; 17: 321-326.
39. Maganga ER. Pneumonia case fatality rate in children under-five : Understanding variations in district hospitals in Malawi. 2004.
40. Leukocytosis and Leukopenia - Infectious Disease and Antimicrobial Agents. 2020.
41. Fanny Vardon-Boues. Platelets Are Critical Key Players in Sepsis. 2019.
42. Mirsaedi M, Peyrani P, Aliberti S, Filardo G, Bordon J, Blasi F, et al. Thrombocytopenia and thrombocytosis at time of hospitalization predict mortality in patients with community-acquired pneumonia.

- Chest. 2010; 137: 416-420.
43. Dunaiceva J, Sabelnikovs O. Incidence and Predictive Value of Thrombocytopenia in Patients with Severe Community Acquired Pneumonia. *Acta Chirurgica Latviensis*. 2015; 15: 35-39.
44. Chiu N-C, Chi H, Peng C-C, Chang H-Y, Huang DT-N, Chang L, et al. Retrospective study of prognostic factors in pediatric invasive pneumococcal disease. *PeerJ*. 2017; 5: e2941.
45. Prevalence-of-pneumonia-and-factors-associated-among-children-259-months-old-in-wondo-genet-district-sidama-zone-snnpr-ethiopia.pdf. 2017.
46. Bekele F, Sinaga M, Quadri JA, Kumar A, Shariff A, Malik T. Factors associated with outcomes of severe pneumonia in children aged 2 months to 59 months at jimma university specialized hospital, southwest Ethiopia. *Curr Pediatr Res*. 2017.

Cite this article

Makanda-Charambira PD, Mujuru HA, Ndhlovu A, Timire C, Nathoo KJ. Mortality in Hospitalized Children Aged 1-59 Months with Pneumonia at Two Tertiary Hospitals in Harare, Zimbabwe. *Ann Pediatr Child Health* 2021; 9(1): 1221.