College of Medicine

An Evaluation of the Prevalence, Characteristics, Outcomes and Predictors of Shock in Children Admitted to Paediatric Wards at Queen Elizabeth Central Hospital in Blantyre, Malawi

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(MBBS)

A dissertation submitted in partial fulfillment of the requirements for the Degree of Master of Medicine in Paediatrics and Child Health

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DECLARATION

I, Mercy Kumwenda, declare that this thesis is original work and has not been submitted for any awards or presented to any other university for marking. The work done here was part of a broader research namely Circulatory Insufficiency in Sub-Saharan African Children (CISSAC) Baseline Audit and Pilot Study. My role in the study was to help come up with the study design and protocol, to collect data, and to analyse and interpret the results of the audit. The study was approved by the College of Medicine Research and Ethics Committee (COMREC) on 7 January 2019 and the study number is P.12/18/2557.

I intend to submit an article based on this work to various peer reviewed journals.

Signed: Mercy K

Date: 01/06/2021

CERTIFICATE OF APPROVAL

The thesis of Mercy Kumwenda approved by the Thesis Examination Committee.

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ABSTRACT

Background: Shock is an important pathophysiological mechanism of death in children in low-resource settings. Despite this, limited data is available on the prevalence, causes and outcome of shock in children in these settings. We performed a prospective study to assess the prevalence, aetiology and risk factors of death in children with shock. This data will be essential to improve guidelines and interventions to reduce shock related mortality in children.

Methods: A prospective descriptive study was performed from 1st February 2019 to 31st January 2020 at Queen Elizabeth Central Hospital (QECH) paediatric department. ALL paediatric admissions screened for shock as defined by FEAST were recruited. The criteria used were impaired consciousness and/or respiratory distress in combination with at least one sign of impaired perfusion: a capillary refill time (CRT) >3 seconds, cold peripheries, weak radial pulse volume and/or severe tachycardia. The WHO definition of shock was used as a comparative definition. Demographic, clinical, laboratory and outcome data were collected from the patient records. Predictors for death were assessed using univariate and multivariate models.

Results: Out of 12840 admissions, 679 had shock resulting in a prevalence of 5.3%. Of these 505 were included in the study of 15/439 (3.4%) fulfilled the more stringent WHO criteria for shock. The median age was 17 months and ranged from 2 months to 16 years. Respiratory distress was reported in 397/488 (81.4%), fever in 383/495 (77.4%), vomiting or diarrhoea was reported in 183/484 (37.8%) and 127/478 (26.6%) respectively and severe malnutrition was documented in 39/471 (8.3%). Severe anaemia (Hb ≤5g/dL) was present in 19/334 (5.7%), and 67/395 (17.7%) tested positive for malaria. HIV prevalence was

27/358 (7.5%) and blood cultures were positive in 8/176 (4.5%). The main clinical diagnoses on discharge were viral/reactive lower respiratory tract diseases 211/470 (44.9%), pneumonia 89/470 (18.8%), gastroenteritis 64/470 (13.6%) and presumed sepsis 57/470 (12.0%). Overall mortality in shocked children was 79/679 (11.6%). We constructed two multivariate models aimed at a) predicting outcome, and b) assessing disease associated outcomes. Clinical factors predictive of death were low coma score (AOR = 4.9, 95% CI = 2.2 - 11.1), delayed CRT (AOR = 3.5, 95% CI = 1.4 – 8.5) and dehydration (AOR 5.9, 95% CI 3.2 – 11.1). The main clinical diagnoses of children that died were presumed sepsis 34/76 (44.7%), gastroenteritis 21/76 (23.7%), severe malaria 13/76 (17.1%), severe malnutrition 9/76 (11.8%) and meningitis 8/76 (10.5%). In the explanatory model for causative factors, having a diagnosis of presumed sepsis (AOR = 9.9, 95% CI = 4.1 – 23.8) or gastroenteritis (AOR = 3.7, 95% CI = 1.8 – 7.4) was associated with increased mortality, while having viral/reactive airways disease was not associated with death (AOR = 0.02, 95% CI = 0.005 – 0.079).

Conclusion: Shock is a common diagnosis in children seen at QECH in Malawi using the modified FEAST criteria, affecting 1 in 18 admissions. The actual prevalence of children with shock may be lower as the FEAST definition we used may have overestimated shock prevalence. This was evidenced by the fact that approximately 40% of those that qualified had a purely respiratory condition and only 3.4% of those who qualified fit the very strict WHO definition. This discrepancy underlines the lack of a valid bedside definition for shock in children in Malawi. In our population, mortality was high at 11%. The children who present with a low BCS, delayed CRT and dehydration were more likely to die. The

diagnoses of sepsis, gastroenteritis and malaria were contributors to death. This might underscore the importance of their prompt treatment.

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CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.1 Definition

Shock is an acute, life-threatening syndrome of circulatory dysfunction resulting in inadequate delivery of oxygen and other nutrients to meet tissue metabolic demands and inadequate removal of tissue waste products. The reduction in tissue oxygen delivery leads to hypoxia and cellular injury. These effects are initially reversible but may rapidly become irreversible, resulting in multi-organ failure and death [1].

Many different definitions of shock exist, and in our setting the World Health Organisation (WHO) definition is commonly used. The WHO definition of *shock* can be measured on the bedside without diagnostic tools and is defined by: cold extremities ***and*** a weak and fast pulse ***and*** a delayed capillary refill time (CRT) of more than 3 seconds. *Severely impaired circulation* is defined as having one or more of cold extremities ***or*** a weak and fast pulse ***or*** a delayed CRT >3 seconds [1]. In high income settings, shock is defined by a combination of clinical variables, haemodynamic variables, oxygen utilisation variables, and/or cellular variables [2].

The definition of shock used in the FEAST trial was *'a severe febrile illness complicated by impaired consciousness (prostration or coma), respiratory distress (increased work of breathing), or both,* ***and*** *with impaired perfusion, as evidenced by one or more of the following: a capillary refill time of 3 or more seconds, lower limb temperature gradient, weak radial-pulse volume, or severe tachycardia'* [3]. The FEAST trial is a recent body of evidence that looked at children with shock in Sub-Saharan Africa and reported some

surprising and unexplained findings concerning the emergency treatment of shock. We used this definition in our study because it signifies an important milestone in understanding shock in children in low resource settings. This definition used for the FEAST trial also has a wider scope and therefore includes children with impaired circulation who may have been missed by using the stricter WHO definition.

1.2 Burden of Disease

Shock is a common emergency that is responsible for significant morbidity and mortality in the paediatric population with an estimated case load of between 400,000 – 500,000 each year [4]. There is however a paucity of prospective data on shock in a hospital population in the African setting. We found four studies that reported data on prevalence in a review we carried out on shock in low-middle income countries (LMIC) - two in a general paediatric hospital population and two in a selection of critically ill paediatric patients. One was a retrospective study done in Kenya which reported a prevalence of 1.5% (n=622) in patients aged between 1 month and 5 years [5]. Another study in India reported the prevalence of shock to be 4.3% (n=98) of all paediatric hospital admissions [6]. There was no prospective data on shock prevalence in a paediatric African hospital population. The two studies done in a critically ill population were from Malawi and Nepal. At Queen Elizabeth Central Hospital (QECH) in Malawi, 42% (N=247) of the most critically ill children admitted through the Paediatric Accident and Emergency (A&E) department resuscitation room in 2005 were found to be shocked [7]. In Nepal, 44.3% (n=54) of all admissions to a paediatric ICU over a 1-year period were due to shock [8].

1.3 Mortality

Mortality in shocked children is very high across many different settings. The pooled mortality estimate in our review of six studies that primarily studied shock was 32.8% (95% CI: 16.4 - 51.6%) [3, 5-9]. The mortality is likely affected by the definition used and severity of the critical illness. For instance, in the FEAST trial the mortality across the different groups was 8.7–12.2% (n=3141) at four weeks post enrollment, and 56 – 69% (n=29) in the severely hypotensive group [3]. The two other studies in critical care settings showed high mortalities of 50% (n=36) in those admitted with septic shock to the PICU in Nepal [8], and 48% (n=247) of the shocked children admitted through the QECH paediatric resuscitation room [7]. In high resource settings, mortality ranges from 0–5% in previously healthy children to 10% in chronically ill children with septic shock [2].

Clinical predictors of death that have been documented in African settings, include coma, bradycardia or severe tachycardia, prolonged CRT and weight <10 kg [10]. Diseases that have been associated with high mortality due to shock in LMICs include sepsis [6,8], diarrhoea and dehydration [5], HIV [7], malaria and severe anaemia [3].

1.4 Statement of the Problem

From this information, it is clear to see that shock is prevalent in critically ill children admitted to hospitals in LMICs, and it contributes greatly to morbidity and mortality**.** Several knowledge gaps exist on this subject and prospectively collected data is scarce. Topics include prospective data on the prevalence and the aetiology of shock in sub-Saharan African children, including Malawi, which may be very different from HIC. Prospective data on

outcome and potential predictors of mortality in African children with shock also needs further studying. We therefore embarked on contributing to narrowing this knowledge gap by performing this study.

CHAPTER TWO: OBJECTIVES

2.1 Broad Objectives

To prospectively determine the prevalence, characteristics, outcome and potential predictors of shock in children admitted during a 12-month period to the paediatric wards at Queen Elizabeth Central Hospital (QECH) in Blantyre Malawi.

2.1 Specific Objectives

2.1.1 Primary objectives

1. To determine the prevalence of shock amongst children admitted to the QECH paediatric wards.
2. To determine the mortality rate in patients presenting in shock

2.1.2 Secondary Objectives

1. To describe the demographic, clinical characteristics and diagnoses of children presenting with shock at QECH.
2. To identify risk factors and explanatory factors associated with a poor outcome.
3. To determine the prevalence and mortality data applying the WHO definition of shock.

CHAPTER THREE: METHODS

3.1 Study Design

We performed a prospective descriptive study of hospital records of children admitted to the QECH paediatric wards. All children that were admitted through the Accident and Emergency (A&E) department were noted and screened for inclusion criteria which were based on a modification of the criteria used in the FEAST trial. This definition was modified as we did not restrict our population to the criteria of 'fever', which is not necessarily a sign of shock. The criteria used were namely:

3.1.1 Inclusion Criteria

Children aged 2 months to 16 years with ***one or both of***:

a. Impaired consciousness (lethargy or Blantyre Coma Score (BCS) <5),

b. Respiratory distress (increased work of breathing),

AND at least one sign of impaired perfusion:

a. Capillary refill time (CRT) > 3 seconds,

b. Lower-limb temperature gradient / cold peripheries,

c. Weak radial pulse volume,

d. Severe tachycardia

>180bpm if < 12months

>160bpm if 1 - < 5years

>140bpm if 5 - <12 years

>120bpm if 12-16 years

3.1.2 Exclusion Criteria

a. Patients with records containing inadequate information to score the inclusion criteria.

b. Parents or guardians of patients that refused informed consent.

3.2 Recruitment Process

This study was performed over a 12-month period (1 February 2019 to 31 January 2020) to take seasonal variability into account. All admissions that came through the paediatric A&E were recorded from the admission book. Patients and their admission charts were followed up at the different wards to assess for eligibility using the above inclusion criteria. Eligibility of patient files was checked against the list of admissions to make sure all patients were accounted for. Once the files were screened, informed consent was obtained from the guardian of each eligible child. A unique numeric identifier was assigned to each enrolled subject. The patient registries in each ward were also used to check for patients who were discharged or died within 24-48hrs of admission before screening could take place, and the files were assessed for eligibility. With permission of COMREC we included eligible patients that had died before parents/guardians could be approached for consent. The screening of patient files was done daily during weekdays and working hours, and the files for patients admitted during weekends and public holidays were screened on the next working day.

3.3 Data Collection and Entry

Data collection was done from the patient hospital record after discharge or death. Recorded data from the patient file was manually entered from the paper medical record to a password-protected electronic case record form (CRF) in an ODK © database (appendix 1).

From the patient file we collected the following:

a. Demographic details
b. Presenting history and duration of symptoms before presentation
c. Clinical signs
d. Results of routine admission investigations carried out by the admitting clinician namely Haemoglobin (Hb) / Packed cell volume (PCV), malaria parasite slide (MPs) / malaria rapid diagnostic test (MRDT), random blood sugar (RBS) and blood cultures (which were confirmed using the laboratory automated database)
e. Admissions
f. Underlying chronic condition(s)
g. Initial resuscitation management at A&E before transfer to the ward
h. Discharge diagnosis / cause of death
i. Outcome (death or discharged alive)

3.4 Statistical Analysis

Data was analysed using IBM SPSS version 23.

The prevalence of shock was calculated by dividing the total number of eligible shock cases by the total number of paediatric admissions as registered in our admission system. The primary analyses were performed using the included population. Secondary analyses were performed applying other shock definitions including:

a. WHO criteria for shock,
b. The full FEAST inclusion criteria which besides shock included severe febrile illness, and
c. Shock excluding reactive/viral lower respiratory tract diagnoses.

Descriptive data on demographic, clinical characteristics and discharge diagnosis was calculated as percentages or means/medians. Groups were compared using Chi-square / Fisher exact test for categorical data and independent t test for numerical data. Outcome (mortality) data was calculated by dividing the total number of deaths by the total eligible cases. Crude associations between predictors of mortality were assessed using univariate analysis (t-test and chi-square). Potential associations with poor outcome ($p < 0.05$) or those that were deemed relevant, were further evaluated using multivariate logistical regression to account for any confounding. We constructed two models one aimed at identifying clinical predictors of mortality and a second model aimed to explain the mortality by assessing diagnoses and other potential causative factors.

CHAPTER FOUR: RESULTS

4.1 Prevalence

A total of 13,995 patients were admitted to the QECH paediatric wards between 1st February 2019 and 31st January 2020. Of these, 12,840 (91.7%) were screened, and 679 (5.3%) fulfilled the enrollment criteria. 505/679 (74.4%) were included in the study (figure 1).

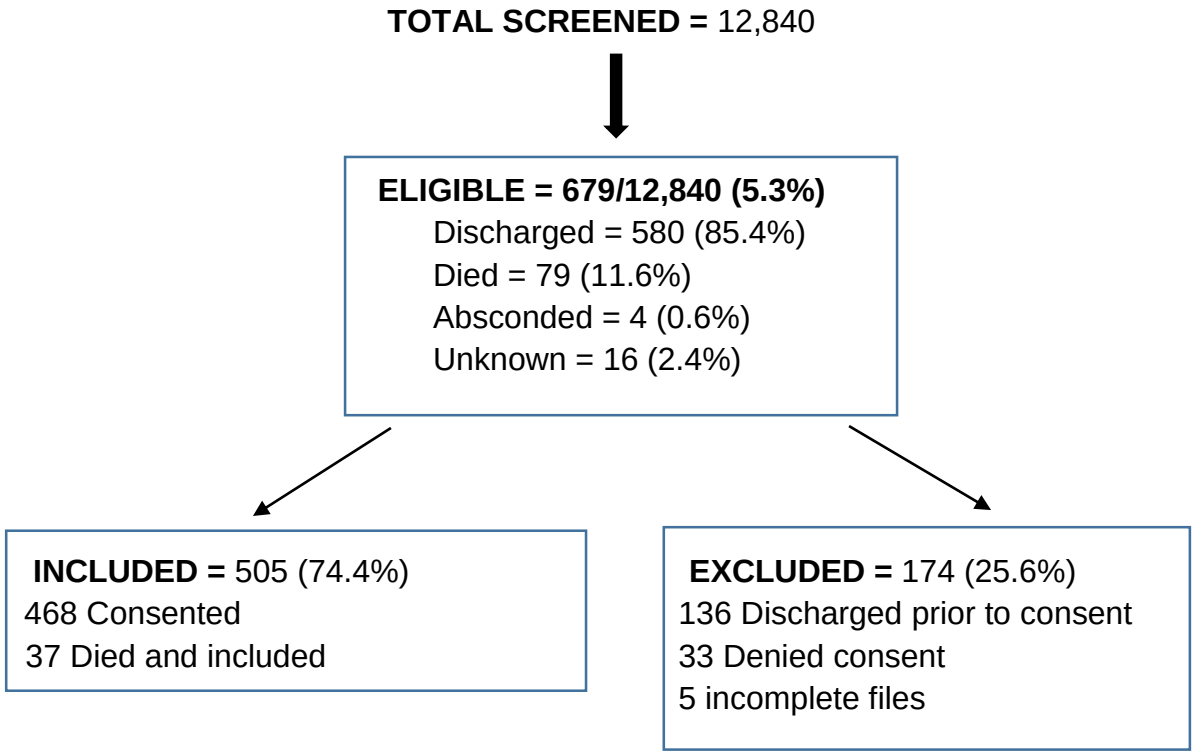

Figure 1: Study Inclusion Policy

From the 505 patients included in the study, 439 (86.9%) could be assessed for fulfillment of WHO criteria for shock. We found the prevalence of shock using the full WHO criteria to be 15/439 (3.4%). The patients that we could assess for full FEAST criteria were 485 (96.0%) and we found that the complete FEAST criteria for febrile shock was fulfilled in 383/485 (77.3%).

During the analysis we noted that primary viral/reactive lower respiratory tract diagnoses were prevalent (190/470 =40.4%) but had a very mild course (mortality 0%) so we decided to exclude this group in a secondary analysis. After exclusion, 280/470 (59.6%) of the patients had a combination of other diagnoses associated with shock that were not viral/reactive lower respiratory diseases.

4.2 Demographics

The age range of participants was 2 months – 16 years with a median age of 17 months. Those under 5 years of age were 410 (81.2%) (figure 2). Males were 282/498 (56.6%).

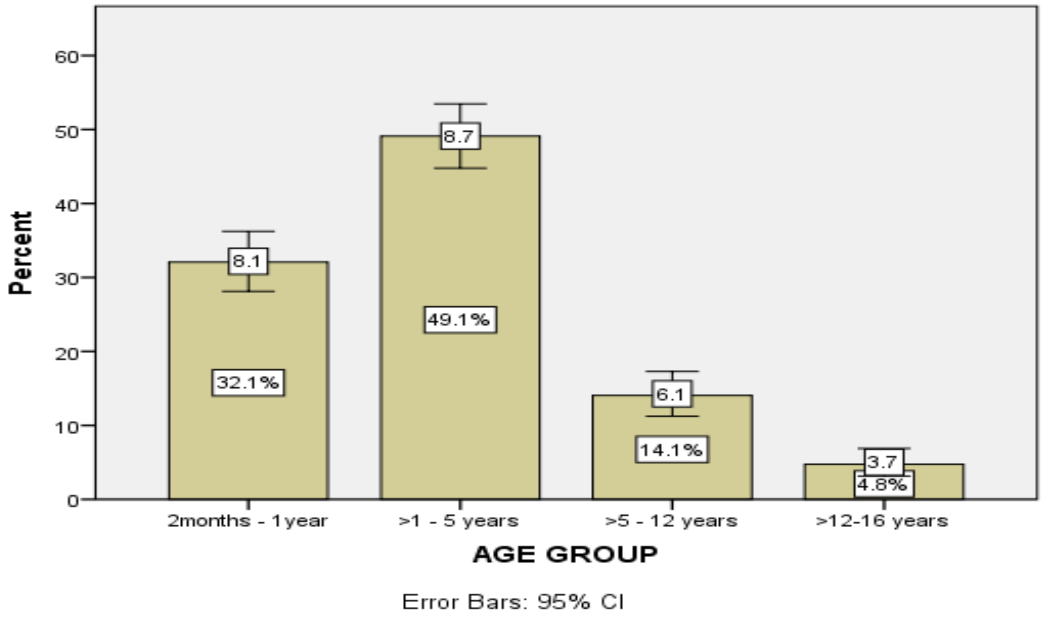

Figure 2: Age Distribution

4.3 Trend of Admissions

Admissions of patients with shock peaked between March – April 2019 (29.3%, n=148). Admissions were highest during working hours with a peak between 9am – 2pm (242/478 =

50.6%). The mean duration of hospital admission was 4.1 days (SD 4.7 days) with a median of 3 days (range 0 – 34 days). In 304 (61.7%) patients, the duration of hospital admission was 3 – 7 days (Figure 3).

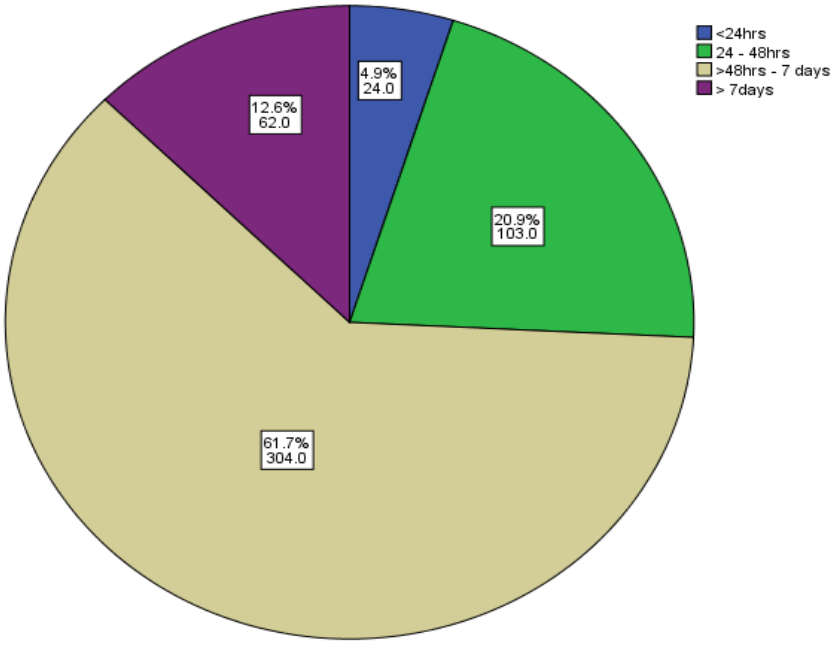

Figure 3:Duration of Hospital Admission

4.4 Presenting Symptoms

The main presenting symptoms were respiratory distress 397/488 (81.4%), fever 383/495 (77.4%) and cough 364/485 (75.1%). Vomiting was present in 183/484 37.8%, diarrhoea in 127/478 (26.6%) and convulsions in 69/476 (14.9%). Three patients (0.6%) with shock presented with trauma. Table 1 shows the frequency of presenting symptoms and the duration of symptoms before presentation to hospital.

Table 1: Frequency and Duration of Presenting Symptoms

SYMPTOM	NUMBER	DURATION (DAYS)	
	(%)	*Mean*	*Range*
RESPIRATORY DISTRESS	397/488 (81.4%)	2.2	59 (1-60)
FEVER	383/495 (77.4%)	2.8	20 (1-21)
COUGH	364/485 (75.1%)	3.8	89 (1-90)
DIFFICULTY IN FEEDING	181/462 (39.2%)	2.8	89(1-90)
VOMITING	183/484 (37.8%)	2.3	27 (1-28)
DIARRHOEA	127/478 (26.6%)	3.4	27 (1-28)
CONVULSIONS	69/476 (14.5%)	1.9	16(1-17)
PALLOR	43/457 (9.4%)	6.3	29 (1-30)
RASH	26/458 (5.7%)	13.9	29(1-30)
OEDEMA	19/463 (4.1%)	13.8	89 (1-90)
JAUNDICE	10/462 (2.2%)	30	179 (1-180)
TRAUMA	3/491 (0.6%)	8.3	20 (1-21)

4.5 Clinical Findings

When we looked at primary qualifying symptoms for recruitment, the most frequent symptom was respiratory distress in 416/504 (82.5%) while lethargy was found in 146/482 (30.3%) of patients and low BCS in 119/485 (24.5%). For the secondary qualifiers, severe tachycardia was the most frequent in 441/492 (89.6%) and delayed CRT (> 3 seconds) was found in 71/457 (15.5%). There was lack of documentation in most of the patient records about cold peripheries and weak radial pulses. However, in the files that reported on this 47/91 (51.6%) had a weak radial pulse and 78/136 (57.4%) had cold peripheries. For the other clinical signs, axillary temperature > 39^0C was present in 86/477 (18.0%) while subnormal (temperature <36.0C) was found in 24/477 (5.0%). Signs of dehydration were present in 72/484 (14.9%) and pallor detected in 97/488 (19.9%). A clinical diagnosis of severe malnutrition was made in 39/471 (8.3%). HIV prevalence was 27/358 (7.5%).

4.6 Laboratory Findings

Random blood sugar (RBS) was checked in 272/505 (53.9%) of the patients, and of these 25 (9.5%) had hypoglycaemia (RBS <2.5mmol/L in well-nourished patients or <3mmol/L in malnourished patients [11]. Blood sugar level > 10mmol/L was found in 45 patients (16.5%). Haemoglobin (Hb) was checked in 334/505 (66.1%) and of these 19 (5.7%) had severe anaemia (Hb ≤ 5g/dL). Moderate anaemia (Hb >5 – 10 g/dL) was found in 129/334 (38.6%). A malaria test (either MPs or MRDT) was done in 395/505 (78.2%) and the result was positive in 67 (17.0%) of all tests done. Blood cultures were taken on clinical indication in 176/505 (34.8%) and 8 (4.5%) of these grew a pathogen namely 3 *Staphylococcus aureus* (including one Methicillin resistant strain), 1 *Salmonella typhimurium*, 1 *Salmonella species*, 1 *Escherichia coli*, 1 *Acinetobacter baumanii* and 1 culture which grew both *Klebsiella pneumonia*e and *Escherichia coli*. In patients with a clinical diagnosis of sepsis, 34/57 (59.6%) had a blood culture collected and 5/34 (14.7%) grew a significant pathogen.

4.7 Comparison of The General Study Population with Sub-Classified Groups

Sub-classification of the demographic, presenting symptoms, clinical signs and laboratory results was done. The patients were divided into those who met the WHO criteria versus those who did not, and those who met the full FEAST criteria versus those who did not. The patients with WHO criteria tended to be younger than those without (mean age of 17.3 months versus 34 months, p=0.03). There was less respiratory distress in those who met the WHO criteria (8/15 = 53.3%) than in those who did not (345/412 = 83.7%, p=0.02) and diarrhoea was more common in WHO criteria (9/15 = 60.0%) than in those without (90/401 = 22.4%, p=0.002). In terms of diagnoses, gastroenteritis and presumed sepsis were more

prevalent in the WHO criteria group ($p < 0.001$). The mortality for those who met WHO criteria (9/15 = 60.0%) was significantly higher than in the group which did not (41/412 = 10.0%, $p < 0.001$).

Severe tachycardia was more common in those who met the full febrile FEAST criteria (342/374 = 91.4%) than those who did not have fever (93/110 = 84.5%, p=0.03). The proportions of weak radial pulse, delayed CRT, cold peripheries and dehydration were similar between the groups which met full febrile FEAST criteria and the ones which did not. Severe pneumonia and malaria were more common in those who met the full febrile FEAST criteria ($p<0.001$). There was no significant difference in mortality between those who met the full febrile FEAST criteria and those who did not. Table 2 shows a summary of these comparisons using the WHO and full febrile FEAST classifications.

Table 2: Comparison between Whole Group Versus WHO and FEAST Criteria

PARAMETER	TOTAL	WHO SHOCK			FULL FEBRILE FEAST CRITERIA		
	(N=505)	YES (N =15)	NO (N = 424)	P value	Full febrile (N=383)	No fever (N=112)	P Value
DEMOGRAPHICS							
AGE (MONTHS)	*Mean* = 34.8 (2-191) *SD* = 42.2	*Mean* = 17.3 (3-85) *SD* = 20.6	*Mean* = 34.0 (2-191) *SD* = 40.4	.035	*Mean* = 33.4 (2-191) *SD* = 40.2	*Mean* = 38.9 (2-184) *SD* = 48.1	.236
SEX (MALE)	282/498 (56.6%)	11/15 (73.3%)	232/417 (55.6%)	.371	219/380 (57.6%)	60/112(53.6%)	.700
COMPLETED VACCINATIONS	264/439 (60.1%)	4/11 (36.4%)	228/369 (61.8%)	.053	208/337 (61.7%)	54/112 (48.2%)	.471
UNDERLYING CONDITIONS	71/456 (15.6%)	3/12 (25%)	59/386 (15.3%)	.410	43/346 (12.4%)	24/101 (23.8%)	.005
PRESENTING COMPLAINTS							
RESPIRATORY DISTRESS	397/488 (81.4%)	8/15 (53.3%)	345/412 (83.7%)	.020	298/370 (80.5%)	93/112 (83%)	.554
FEVER	383/495 (77.4%)	11/15 (73.3%)	323/417 (77.5%)	.754	383/383 (100%)	0/112 (0.0%)	N/A
COUGH	364/485 (75.1%)	4/14 (28.6%)	324/411 (78.8%)	.000	277/369 (75.1%)	82/111 (73.9%)	.800
VOMITING	183/484 (37.8%)	11/15 (73.3%)	144/406 (35.5%)	.005	152/368 (41.3%)	30/112 (26.8%)	.006
DIFFICULTY IN FEEDING	181/462 (39.2%)	11/15 (73.3%)	145/388 (37.4%)	.007	153/351 (43.6)	26/108 (24.1%)	.000
DIARRHOEA	127/478 (26.6%)	9/15 (60.0%)	90/401 (22.4%)	.002	99/363 (27.3%)	25/111 (22.5%)	.319
CONVULSIONS	69/476 (14.5%)	4/15 (26.7%)	53/401 (13.2%	.136	58/363 (16%)	10/110 (9.1%)	.071
PALLOR	43/457 (9.4%)	2/14 (14.2%)	33/384 (8.6%)	.353	32/344 (9.3%)	10/111 (9.0%)	.926
RASH	26/458 (5.7%)	3/14 (21.3%)	19/386 (4.9%)	.035	23/346 (6.6%)	3/110 (2.7%)	.122
EDEMA	19/463 (4.1%)	1/14 (7.1%)	14/391 (3.6%)	.416	9/249 (2.6%)	10/112 (8.9%)	.003
JAUNDICE	10/462 (2.2%)	1/14 (7.1%)	7/390 (1.8%)	.248	8/349 (2.3%)	2/111 (1.8%)	.758
TRAUMA	3/491 (0.6%)	0/15 (0.0%)	1/411 (0.2%)	1.000	1/374 (0.3%)	2/111 (1.8%)	.070
CLINICAL SIGNS							
FEVER >39^{0}C	86/477 (18%)	3/14 (21.4%)	69/399 (17.3%)	.131	84/369 (22.8%)	2/100 (1.8%)	.000
HYPOTHERMIA <36^{0}C	24/477 (5%)	2/14 (14.3%)	17/399 (4.3%)		13/369 (3.5%)	10/100 (10.0%)	
RESPIRATORY DISTRESS	416/504 (82.5%)	11/15 (73.3%)	357/424 (84.2%)	.280	309/383 (80.7%)	98/111 (88.3%)	.064
PROSTRATION/LETHARGY	146/482 (30.3%)	14/15 (93.3%)	98/405 (24.2%)	.000	113/365 (31.0%)	28/107 (26.2%)	.341
COMA (BCS ≤4)	119/485 (24.5%)	13/15 (86.7%)	79/408 (19.4%)	.000	87/371 (23.5%)	26/104 (25%)	.743

SEVERE TACHYCARDIA	441/492 (89.6%)	12/15 (80.0%)	382/419 (91.2%)	.152	342/374 (91.4%)	93/110 (84.5%)	.035
WEAK RADIAL PULSE	47/91 (51.6%)	15/15 (100.0%)	18/59 (30.5%)	.000	35/69 (50.7%)	10/20 (50%)	.954
CRT >3 SECONDS	71/457 (15.5%)	15/15 (100%)	23/403 (5.7%)	.000	49/346 (14.2%)	18/101 (17.8%)	.365
COLD PERIPHERIES	78/136 (57.4%)	15/15(100.0%)	40/96 (41.7%)	.000	55/98 (56.1%)	19/33 (57.6%)	.884
DEHYDRATION	72/484 (14.9)%	8/15 (53.3%)	38/407 (9.3%)	.000	52/365 (14.2%)	16/109 (14.7%)	.910
PALLOR	97/488 (19.9%)	8/15 (53.3%)	68/411 (16.5%)	.002	75/370 (20.3%)	20/108 (18.5%)	.688
JAUNDICE	15/488 (3.1%)	1/15 (6.7%)	10/412 (2.4%)	.328	12/369 (3.3%)	3/109 (2.8%)	.793
EDEMA	18/490 (3.7%)	0/15 (0.0%)	14/414 (3.4%)	1.000	7/369 (1.9%)	10/111 (9.0%)	.000
CARDIAC SIGNS	25/491 (5.1%)	0/14 (0.0%)	19/413 (4.6%)	1.000	14/373 (3.8%)	10/108 (9.3%)	.021
POOR NUTRITION	39/471 (8.3%)	4/15 (26.7%)	27/398 (6.8%)	.022	29/355 (8.2%)	9/107 (8.4%)	.739
LABORATORY RESULTS							
HIV INFECTED	27/358 (7.5%)	2/13 (15.3%)	21/303 (6.9%)	.001	22/270 (8.1%)	4/78 (5.1%)	.277
HIV EXPOSED	31/358 (8.7%)	5/13 (38.4%)	22/303 (7.3%)		26/270 (9.6%)	4/78 (5.1%)	
RBS <2.4 OR <3MMOL/L	25/272 (9.2%)	6/15 (40.0%)	13/214 (6.1%)	.001	17/205 (8.3%)	6/61 (9.8%)	.856
RBS > 10MMOL/L	45/272 (16.5%)	2/15 (13.3%)	32/214 (15.0%)		33/205 (16.1%)	11/61 (18.0%)	
HB ≤5G/DL	19/334 (5.7%)	1/13 (7.7%)	15/276 (5.4%)	.552	16/260 (6.2%)	2/70 (2.9%)	.047
HB >5 - < 10G/DL	129/334 (38.6%)	6/13 (46.2%)	107/276 (38.8%)		108/260 (41.5%)	20/70 (28.6%)	
POSITIVE MALARIA TEST	67/395 (17%)	4/14 (28.6%)	54/333 (16.2%)	.265	64/317 (20.2%)	3/75 (4.0%)	.001
POSITIVE BLOOD CULTURE	8/176 (4.5)	0/8 (0%)	7/136 (5.1%)	1.000	7/152 (4.6%)	1/23 (4.3%)	.956
DIAGNOSTIC CATEGORY							
BRONCHIOLITIS/ASTHMA/VIW	190/470 (40.4%)	0/15 (0.0%)	179/392 (45.7%)	.000	137/356 (38.5%)	49/104 (47.1%)	.658
SEVERE PNEUMONIA	67/470 (14.3%)	0/15 (0.0%)	60/392 (15.3%)	.101	60/356 (16.9%)	6/104 (5.8%)	.005
GASTROENTERITIS	53/470 (11.3%)	6/15 (40.0%)	31/392 (7.9%)	.000	38/356 (10.7%)	13/104 (12.5%)	.602
PRESUMED SEPSIS	27/470 (5.7%)	4/15 (26.7%)	14/392 (3.6%)	.000	20/356 (5.6%)	6/104 (5.8%)	.953
MALARIA	59/470 (12.6%)	4/15 (26.7%)	46/392 (11.7%)	.084	56/356 (15.7%)	3/104 (2.9%)	.001
NEUROLOGICAL DISEASE	25/470 (5.3%)	0/15 (0.0%)	20/392 (5.1%)	.370	19/356 (5.3%)	5/104 (4.8%)	.831
CARDIAC DISEASE	19/470 (4.0%)	0/15 (0.0%)	16/392 (4.1%)	.425	10/356 (2.8%)	8/104 (7.7%)	.024
MORTALITY	76/505 (15.0%)	9/15 (60%)	41/412 (10.0%)	.000	55/376 (14.6%)	18/107 (16.8%)	.576

We noticed that there was a large proportion of children with viral lower respiratory tract disease and/or reactive airways disease in our shock population (190/470=40.4%). To better understand the difference between these children with and without viral/reactive lower respiratory diagnoses we compared their characteristics. For those without viral/reactive airway disease, diarrhoea, convulsions and fever > 39^0C were more common than those with primary respiratory disease (all $p < 0.05$, Table 3). The non-viral/reactive airways disease group were also more likely to have a weak radial pulse, cold peripheries, dehydration and prolonged CRT >3seconds (all $p < 0.05$, Table 3). There were no cases of severe anaemia in the predominantly viral/reactive airways disease group, and none of the patients in that category died. The differences in the demographic, presenting symptoms, clinical and laboratory data for these are summarised in table 3.

Table 3: Comparison between Primary Viral/Reactive Airways Disease and Other Diagnoses

PARAMETER	TOTAL (N = 505)	VIRAL / REACTIVE AIRWAYS DISEASE		
		NO (N = 280)	YES (N = 190)	P value
AGE (MONTHS)	*Mean* = 34.8 (2-191) *SD* = 42.216	*Mean* = 39.9 (2-187) *SD* = 47.642	*Mean* = 26.1 (2-191) *SD* = 31.028	.003
SEX (MALE)	282/498 (56.6%)	150/276 (54.3%)	110/187 (58.8%)	.341
COMPLETED VACCINES	264/439 (60.1%)	151/239 (63.2%	96/187 (50.5%)	.053
UNDERLYING CONDITIONS	71/456 (15.6%)	46/260 (17.7%)	22/167 (13.2%)	.213
PRESENTING COMPLAINT				
RESPIRATORY DISTRESS	397/488 (81.4%)	185/268 (69.0%)	186/187 (99.5%)	.000
FEVER	383/495 (77.4%)	219/274 (79.9%)	137/186 (73.7%)	.115
COUGH	364/485 (75.1%)	151/263 (57.4%)	186/189 (98.4%)	.000
VOMITING	183/484 (37.8%)	123/272 (43.9%)	46/180 (25.6%)	.000
DIFFICULTY IN FEEDING	181/462 (39.2%)	124/257 (48.2%)	43/175 (24.6%)	.000
DIARRHOEA	127/478 (26.6%)	97/267 (36.3%)	18/179 (10.1%)	.000
CONVULSIONS	69/476 (14.5%)	64/264 (24.2%)	1/182 (0.5%)	.000
PALLOR	43/457 (9.4%)	39/253 (15.4%)	1/175 (0.6%)	.000
RASH	26/458 (5.7%)	17/253 (6.7%)	9/176 (5.1%)	.493
EDEMA	19/463 (4.1%)	19/255 (7.5%)	0/177 (0.0%)	.000
JAUNDICE	10/462 (2.2%)	10/254 (3.9%)	0/178 (0.0%)	.007
TRAUMA	3/491 (0.6%)	3/277 (1.1%)	0/181 (0.0%)	.160
CLINICAL SIGNS				
FEVER >39^{0}C	86/477 (18%)	70/268 (26.1%)	11/178 (6.2%)	.000
HYPOTHERMIA <36^{0}C	24/477 (5%)	19/268 (7.1%)	4/178 (2.2%)	.000
RESPIRATORY DISTRESS	416/504 (82.5%)	199/279 (71.3%)	189/190 (99.5%)	
PROSTRATION/LETHARGY	146/482 (30.3%)	137/266 (51.5%)	1/182 (0.5%)	.000
COMA (BCS ≤4)	119/485 (24.5%)	111/269 (41.3%)	2/181 (1.1%)	.000
SEVERE TACHYCARDIA	441/492 (89.6%)	221/268(82.5%)	188/190 (98.9%)	.000
WEAK RADIAL PULSE	47/91 (51.6%)**	46/78 (59.0%)	1/12 (8.3%)	.001
CRT >3SECONDS	71/457 (15.5%)	68/257 (26.5%)	0/167 (0.0%)	.000
COLD PERIPHERIES	78/136 (57.4%)**	76/107 (71.0%)	0/22 (0.0%)	.000
DEHYDRATION	72/484 (14.9)%	67/265 (25.3%)	0/184 (0.0%)	.000
PALLOR	97/488 (19.9%)	89/267 (33.3%)	2/186 (1.1%)	.000
JAUNDICE	15/488 (3.1%)	14/267 (5.2%)	0/186 (0.0%)	.002
EDEMA	18/490 (3.7%)	18/269 (6.7%)	0/186 (0.0%)	.000
CARDIAC SIGNS	25/491 (5.1%)	22/274 (8.0%)	1/183 (0.5%)	.000
POOR NUTRITIONAL STATUS	39/471 (8.3%)	37/261 (14.2%)	0/177 (0.0%)	.000
LABORATORY RESULTS				
HIV INFECTED	27/358 (7.5%)	24/207 (11.6%)	2/128 (1.6%)	.002
HIV EXPOSED	31/358 (8.7%)	21/207 (10.1%)	10/128 (7.8%)	
RBS <2.4 OR <3MMOL/L*	25/272 (9.2%)	25/195 (12.8%)	0/57 (0.0%)	.017
RBS > 10MMOL/L	45/272 (16.5%)	31/195 (15.9%)	10/57 (17.5%)	
HB ≤5G/DL	19/334 (5.7%)	16/207 (7.7%)	0/106 (0.0%)	.000
HB >5 - < 10G/DL	129/334 (38.6%)	96/207 (46.4%)	30/106 (28.3%)	
POSITIVE MALARIA TEST	67/395 (17%)	61/232 (26.3%)	3/134 (2.2%)	.000
POSITIVE BLOOD CULTURE	8/176 (4.5)	7/146 (4.8%)	1/17 (5.9%)	.844
MORTALITY	76/505 (15.0%)	75/280 (26.8%)	0/190 (0.0%)	.000

4.8 Diagnoses

Of the participants, 470/505 (93.1%) had a discharge / death diagnosis recorded. Of the missing diagnoses, 4 files had no clearly recorded diagnosis, and in 31 the section with the final diagnosis could not be found. 190/470 (40.4%) had more than one diagnosis therefore there was overlap in some of the diagnostic categories.

The predominant diagnoses were viral/reactive airways diseases (bronchiolitis / asthma / viral induced wheeze) making up 211/470 (44.9%) of all diagnoses. Pneumonia was recorded in 89/470 (18.8%), gastroenteritis in 64/470 (13.6%), presumed sepsis in 57/470 (12.0%) malaria in 57/470 (12.0%), anaemia in 29/470 (6.1%), severe malnutrition in 21/470 (4.4%), congenital / rheumatic heart disease in 17/470 (3.6%) meningitis 15/470 (3.2%), tuberculosis 12/470 (2.5%) and cerebral malaria 10/470 (2.1%). The diagnostic groups of the patients are illustrated in Table 2 and the full list of patient diagnoses and their frequencies is in Appendix 2.

4.9 Clinical Management

4.9.1 Fluid Management

Bolus fluids were given to 83/505 (16.4%) of all patients and in 13/15 (86.7%) of those with WHO criteria. The most common fluid given was Ringers Lactate (42/83 = 50.6%). In the majority of patients, the total amount of fluid boluses administered was 30ml/kg and in most of these, WHO plan C for severely dehydrated patients was administered (Figure 4).

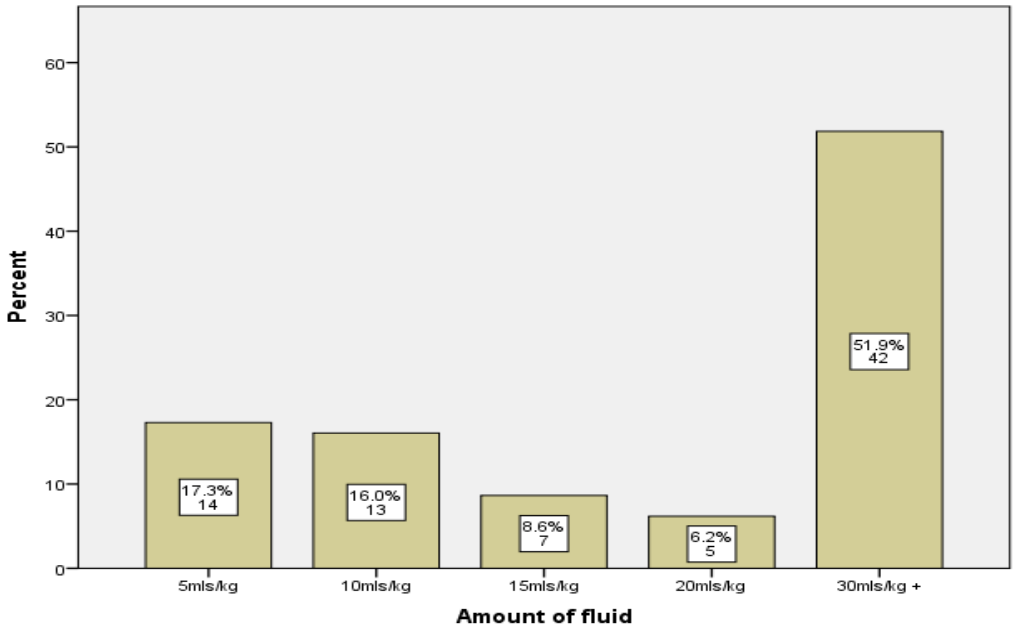

Figure 4: Amount of Bolus Fluid Given

4.9.2 Blood Transfusion

48/505 patients (9.5%) had a blood transfusion with 70.8% being given whole blood and 20.1% receiving packed red blood cells. One patient had a transfusion of fresh frozen plasma. Of those who had severe anaemia (haemoglobin ≤ 5 g/dL), 17/19 (89.5%) received a transfusion on admission. 22/107 (17.6%) of those who had haemoglobin between >5 – 10 g/dL and 6/180 (3.2%) of those who had haemoglobin > 10g/dL got transfused.

4.9.3 Antibiotic Administration

Antibiotics were prescribed in 231/505 patients (45.7%). The combination of crystalline penicillin with gentamycin was the most frequently given, followed by ceftriaxone. This is illustrated in figure 5. Eighty-two percent (47/57) of patients with a clinical diagnosis of sepsis received antibiotics on admission.

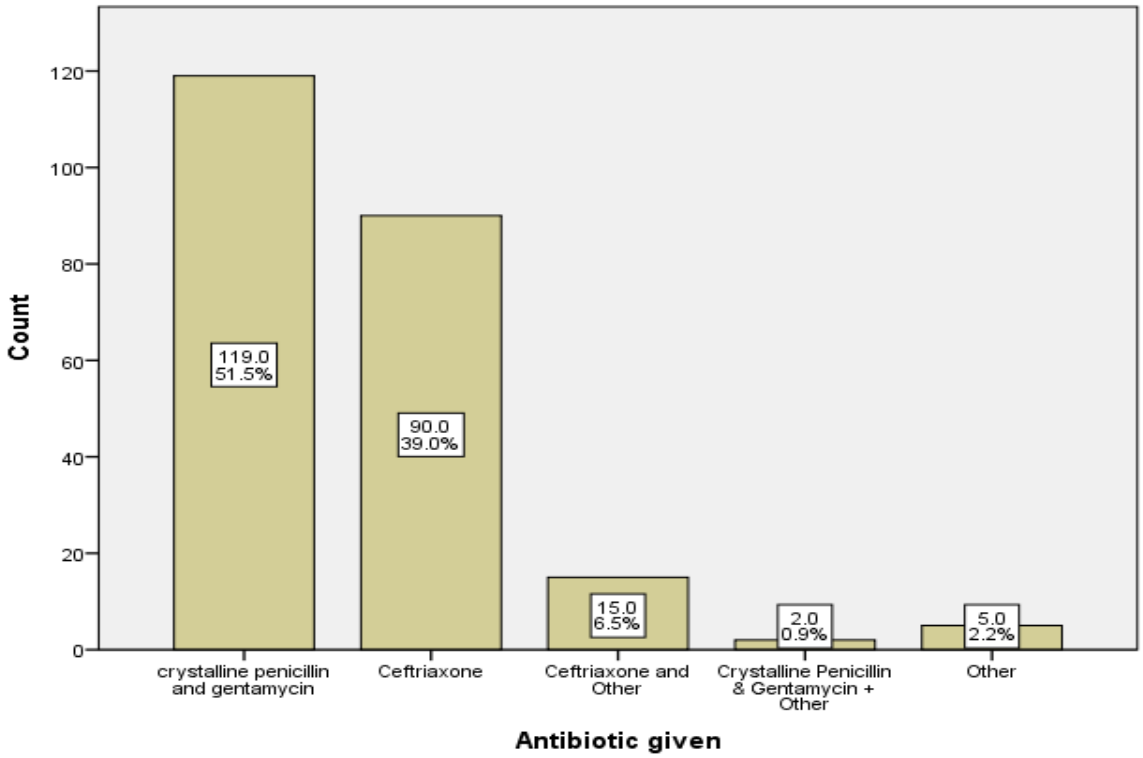

Figure 5: Types of Antibiotics Prescribed

4.9.4 Antimalarial Use

77/505 (15.2%) of patients were treated with an antimalarial, of which 65 (84.4%) had a positive malaria test. Of these, 75 (97%) received antimalarial treatment, with Artesunate being the main drug used except in one patient who received Lumefantrine Artemether.

4.9.5 Other Treatments

An intraosseous needle was inserted in 17/505 patients (3.4%) while Cardiopulmonary Resuscitation (CPR) was performed in 4/505 patients (0.8%) on admission to the A&E.

4.10 Outcomes

The overall mortality in all eligible participants was 79/679 (11.6%). For those included in the study, 76/505 (15.4%) died, 413/505 (83.8%) were discharged, 4/505 patients (0.6%) absconded from hospital and 16/505 (2.4%) were lost to follow up.

4.10.1 Time to death

Twenty-one (27.6%) of all deaths happened within the first 24 hours of admission and more than half (42/76 = 55.2%) of all the deaths had occurred within 48 hours (Figure 6).

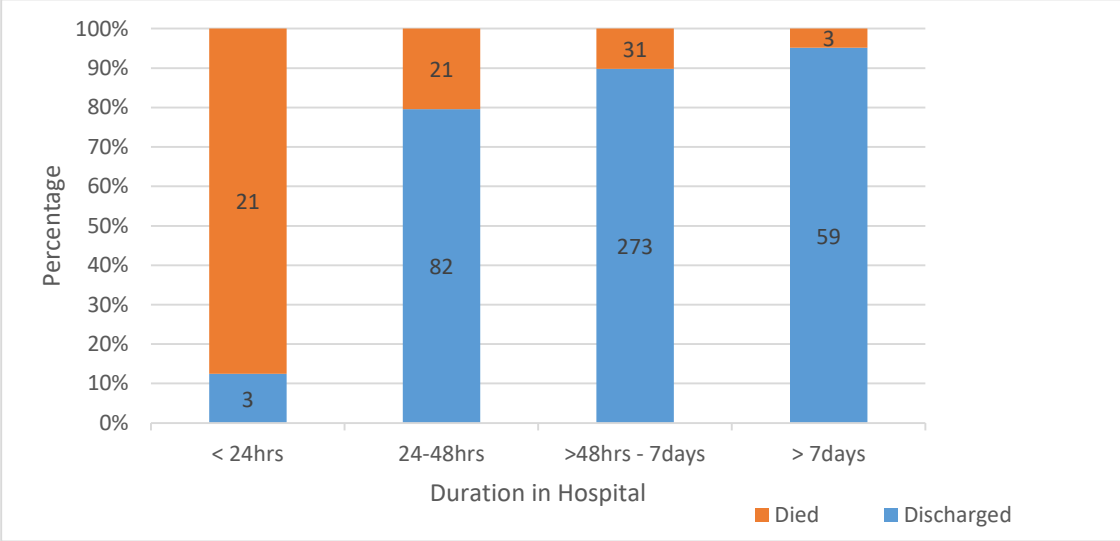

Figure 6:Proportion of Deaths According to Duration of Hospital Admission

4.10.2 Diagnoses in the Deaths

Amongst children that died the most common clinical diagnoses were presumed sepsis, gastroenteritis and malaria as shown in table 4. Other diagnoses that may have contributed to death included severe malnutrition, meningitis, pneumonia, heart disease, anaemia and hypoglycaemia.

Table 4: Final Diagnosis in Shocked Children that Died

DEATH DIAGNOSIS	Frequency - N (%)
Presumed Sepsis	34 (44.7)
Gastroenteritis	21 (27.6)
Malaria	13 (17.1)
Severe Malnutrition	9 (11.8)
Meningitis	8 (10.5)
Severe Pneumonia	6 (7.9)
Congenital / Rheumatic Heart Disease	6 (7.9)
Anemia	6 (7.9)
Hypoglycaemia	4 (5.3)
Encephalitis	4 (5.3)

4.11 Predictors of Mortality

To understand the mortality, we compared the characteristics of patients that died versus those who survived using univariate analysis (Table 5). The parameters that were found to be associated with death in the univariate analysis were further analysed using multivariate logistical regression. Two separate models were created to assess risk factors for mortality on admission and to assess potential causative factors (diagnoses).

4.11.1 Clinical and Laboratory Predictors of Mortality (Risk Factors)

From the univariate analysis, clinical features that tended to have increased mortality were poor nutritional status, low BCS, CRT >3seconds, weak radial pulse, cold peripheries and dehydration (all $p < 0.05$, table 5). In a multivariate logistical regression model (Table 6), low BCS (AOR = 6.5, 95% CI = 3.7 – 11.6), CRT>3 sec (AOR = 10.1, 95% CI = 5.4 – 19.0) and dehydration (AOR = 6.0, 95% CI = 3.2 – 11.1) remained significant as predictors of

poor outcome. Having severe tachycardia was observed in participants who had low mortality (AOR = 0.14, 95% CI =0.07 – 0.27). For the laboratory parameters, a low RBS and positive blood culture were observed in participants with increased mortality ($p<0.05$) on univariate analysis (Table 5). Participants with anaemia showed no corresponding increase in mortality ($p=2.85$).

Table 5: Univariate Analysis Showing Potential Mortality Associations

PARAMETER		ALIVE		DIED		P value
		Count	Percent	Count	Percent	
Age	2months - 1year	132	31.7%	29	38.2%	
	>1 - 5 years	207	49.6%	32	42.1%	.646
	>5 - 12 years	59	14.1%	11	14.5%	
	>12-16 years	19	4.6%	4	5.3%	
Sex	Female	172	41.7%	37	50.0%	.187
	Male	240	58.3%	37	50.0%	
HIV Infection	Yes	23/304	7.6%	4/48	8.3%	.601
Poor Nutrition	Yes	23/391	5.9%	16/68	23.5%	.000
Pre-existing Disease	Yes	54/379	14.2%	15/69	21.7%	.113
Impaired circulation	Yes	48/78	61.5%	55/62	88.7%	.000
WHO shock	Yes	6/377	1.6%	9/50	18.0%	.000
Reduced BCS	0-4	73/401	18.2%	44/72	61.1%	.000
Respiratory Distress	Yes	360/417	86.3%	46/75	61.3%	.000
Severe Tachycardia	Yes	388/414	93.7/5	41/66	62.1%	.000
Weak Radial Pulse	Yes	18/54	33.3%	29/36	80.6%	.000
CRT	> 3 seconds	31/373	8.3%	39/72	54.2%	.000
Cold peripheries	Yes	28/77	36.4%	49/57	86.0%	.000
Dehydration	Yes	37/398	9.3%	34/74	45.9%	.000
Blood Glucose	<2.5 / <3mmol/L	9/191	4.7%	16/71	22.5%	
	>10 mmol/L	25/191	13.1%	17/71	23.9%	.000
Degree of Anaemia	Hb >10g/dL	150	56.4%	28	48.3%	
	Hb >5 - 10g/dL	100	37.6%	28	48.3%	.285
	Hb ≤5g/dL	16	6.0%	2	3.4%	
Malaria Test	Positive	51/325	15.7%	14/58	24.1%	.114
Blood Culture	Positive	3/134	2.2%	5/40	12.5%	.007
Diagnostic Group	Bronchiolitis/Asthma/VIW	190	50.8%	0	0.0%	.000
	Severe Pneumonia	65	17.4%	2	3.0%	.002
	Gastroenteritis	32	8.6%	21	31.8%	.000
	Presumed Sepsis	10	2.7%	17	25.8%	.000
	Cardiac disease	12	3.2%	7	10.6%	.011
	Malaria	47	12.6%	12	18.2%	.326
	Neurological disease	18	4.8%	7	10.6%	.091

4.11.2 Diseases Presenting with Increased Mortality (Causative)

Diagnoses which presented with increased mortality were gastroenteritis, presumed sepsis and cardiac disease (all $p<0.01$). Having a diagnosis of viral / reactive airways disease or pneumonia was associated with reduced mortality (all $p < 0.01$). A diagnosis of malaria or neurological disease did not show a significant effect on mortality. In a multivariate logistical regression model presumed sepsis (AOR = 9.9, 95% CI = 4.1– 23.7) and gastroenteritis (AOR = 3.7, 95% CI = 1.85 – 7.4) showed increase in death. Having viral / reactive airways disease like bronchiolitis/asthma/viral induced wheeze did not result in death (AOR = 0.019, 95% CI = 0.005 – 0.079). This is illustrated in table 6 and table 7. All the diagnoses labelled were based on clinical conclusion of the attending clinicians.

Table 6: Multivariate Logistical Regression for Mortality Predictors

Parameter	Univariate		Predictive Multivariate Model	
	OR	95% CI	OR	95% CI
Impaired Consciousness (BCS 1-4)	7.1	4.1 – 12.0	6.5	3.7 – 11.6
CRT >3seconds	13.0	7.2 – 23.6	10.1	5.4 – 19.0
Severe Tachycardia [a]	0.1	0.06 – 0.21	0.14	0.07– 0.27
Clinically Dehydrated	8.293	4.7 – 14.6	6.0	3.2 – 11.1

[a] The parameters for severe tachycardia are as used in the inclusion criteria.

Table 7: Multivatiate Logistical Regression for Mortality

Parameter	Univariate		Multivariate Model (Causative)	
	OR	95% CI	OR	95% CI
Presumed Sepsis	11.3	4.9 – 25.8	9.9	4.1 – 23.8
Gastroenteritis	4.4	2.4 – 8.2	3.7	1.8 – 7.4
Cardiac Disease	3.3	1.2 – 8.6	2.3	0.7 – 7.4
Viral / reactive airways disease	0.02	0.004 – 0.06	0.02	0.005 – 0.08

CHAPTER FIVE: DISCUSSION

5.1 Introduction

The 5.3% prevalence of shock found in paediatric admissions at QECH highlights that shock is a common presenting feature in children in hospitals in Malawi. Several overlapping diseases were found in children presenting with shock at QECH and mortality was high especially in patients presenting with presumed sepsis and gastroenteritis.

5.2 Prevalence of Shock

Our prevalence of 5.3% was slightly higher than what was shown in other studies, namely 1.5% [5] to 4.3% [6]. A retrospective audit similar to ours done in Kenya by a group of hospitals which collected data from charts of children aged 1 month to 5 years, found that shock was recorded as a feature in 1.5 % (range 0.2–3.2 % per hospital) [5]. Our prevalence of 5.3% is higher than that found in Kenya. This may be explained by the fact that we used a different criterion for shock and may have gotten a wider range of patients including those who had viral/reactive lower respiratory tract diseases who were misclassified as shock and thus an over-estimated prevalence. The more accurate prevalence of shock at QECH may therefore be lower (approximately 3%) if we restricted the definition of shock by excluding respiratory cases.

Due to the prospective design of our study, we would have potentially recruited more patients which might have been missed by the retrospective studies. The number of patients in our study who were labelled as having shock in the clinical records was 36/470 which would give an estimated prevalence of 36/12840 (0.3%). This might highlight the challenge

of using retrospective clinical notes analysis to calculate the prevalence of shock as there is potential for significant underreporting due to lack of active case finding. There may also be differences in data collection methods and patient selection since they excluded children with severe malnutrition, surgical/burns and age >5years. The prevalence in retrospective studies therefore may not be similar to ours. However irrespective of the definition used, shock is a relatively common condition in LMICs affecting a substantial proportion of children with an estimated prevalence of approximately 1 in 20 admitted children according to the feast definitions.

5.3 Patient Characteristics

5.3.1 Demographics

The majority of our study participants were under five years of age, because there is a high burden of disease in this age group. Our data corroborates with the two other studies done in an African setting, in which Mbevi et al found a median age of 15 months in Kenya and the FEAST trial reported a median age of 24 months [3,5]. Another contributing reason for having large numbers of young age in our study was that most of our patients had a diagnosis of bronchiolitis / asthma / viral induced wheeze which are common in the under-five age-group. When this group was separated from the other patients, there was a significant difference in mean age from 26.1 months in the viral/reactive lower respiratory disease group to 39.9 months in the group which did not have these diagnoses (p=0.003).

5.3.2 Presenting Symptoms and Clinical Signs

The qualifying symptoms for inclusion in our study were either impaired consciousness and/or respiratory distress. The majority of our patients had respiratory distress (397/488 = 81.4%) as a qualifier to be included into the study while impaired consciousness was present in 30.3% of those who qualified (146/482). The clinical sign of severe tachycardia was present in 441/492 (89.6%). Other clinical signs for inclusion were less prevalent, with delayed CRT being present in 71/457(15.5%), weak radial pulse in 47/91 (51.6%) and cold peripheries present in 78/136 (57.4%). Weak radial pulse and cold peripheries were documented for less than one fifth and less than one third of the study population respectively. This makes it difficult to have a more accurate picture of the full clinical parameters of children presenting in shock in our setting.

Respiratory distress and tachycardia are common in ill children and may be non-specific to any particular disease. This is shown in our analysis where we found that the inclusion criteria of respiratory distress combined with a clinical sign of severe tachycardia captured more non-shocked children who had viral / reactive lower respiratory tract diseases like asthma, bronchiolitis and viral induced wheeze (190/470=40.4%, Table 3). The inclusion of these patients led to an over-estimation of the prevalence of shock and may also have affected the descriptive data on the population of children with truly impaired circulation and shock.

A history of fever was quite common and present in 383/495 (77.4%), making almost 80% of our study population meet the full febrile FEAST criteria. Other prominent symptoms

were difficulty in feeding (181/462=39.2%), vomiting (183/484 = 37.8%) and diarrhoea (127/478=26.6%). Gastrointestinal symptoms are therefore quite common in ill children with shock.

When we separated the purely viral/reactive lower respiratory disease group from the study population, we found that the patients *without* pure viral/reactive lower respiratory tract disease were more likely to be sicker. They had a higher incidence of a history of convulsions, diarrhoea/vomiting, difficulty feeding and pallor (all $p < 0.001$). Clinically, they presented more with prostration/lethargy, reduced BCS, fever $>39^0$C or hypothermia, pallor, poor nutrition, and signs of severely impaired perfusion (all $p< 0.001$, Table 3). Delayed CRT was present in only 71/457 (15.5%) of the combined patient population, but the incidence increased to 68/257 (26.5%) when we separated out the viral/reactive lower respiratory tract disease. FEAST found a comparable delayed CRT in 26% (N = 819) of study participants. Children in shock therefore have a wide array of clinical symptoms and signs which indicate severe illness but are not always easy to distinguish from patients without shock.

5.4 Other Definitions of Shock

This study has revealed the challenges of making a diagnosis of shock. As noted from our results, using the Modified FEAST criteria for circulatory impairment, nearly half of our participants were diagnosed as having viral / reactive lower respiratory tract disease. More than 98% of these patients had respiratory distress with severe tachycardia as the only sign of circulatory impairment (Table 3). The tachycardia may thus also reflect the severity of

their respiratory effort and they may have falsely labelled the patients as having ‘shock’. The underlying pathophysiology of disease would however not be related to shock or severely impaired circulation. This point highlights that the definition we, and others, used for ‘shock’ may not be accurate, and was possibly too broad leading to over diagnosis of shock in our participants. There is need to have conclusive diagnostic tool to ascertain this.

5.4.1 Full Febrile FEAST Definition

The full febrile FEAST definition for shock applied to 77.4% of our study population who had fever as well as other signs of shock. We did not use the full febrile FEAST definition in our study because shock can be present in non-febrile patients from other non-infectious causes, hence we did not want to limit out study group by selecting out other important non-febrile causes of shock. However, apart from fever, there were not many other significant differences in demographic, clinical or outcome characteristics between the group which fulfilled the full febrile FEAST criteria and the group which did not (Table 2).

In light of this, it is possible that the full febrile FEAST definition of impaired circulation may also have recruited other children who did not have shock due to the broadness of the definition. The full febrile FEAST definition is therefore sensitive for identifying children with potential shock, but may have resulted in identification of false positive ‘shock’ cases if diagnosis was made strictly based on that definition.

Approximately three quarters of the participants who had purely viral/reactive lower respiratory tract disease had come with a history of fever, thus meeting the full FEAST

criteria of severe febrile illness upon presentation. It is however important to note that only 0.5% of these patients had lethargy (compared to 51.5% in the non-respiratory group {p= 0.000}, Table 3). More studies to look into these parameters would be warranted in order to come closer to an optimal bedside definition of shock for use in LMICs.

5.4.2 WHO Definition of Shock

In our study the patients who met WHO criteria for shock were few (n=15, 3.4%) of study participants and 16/12840 (0.1%) of all the admissions, which is comparable to the prevalence found in Kenya by Mbevi et al [5]. who also had a prevalence of 0.1%. In the FEAST study, WHO shock was found in 65/3170 (2.1%) of the enrolled participants [12], which was in line with the 3.4% in our study population. Mortality was significantly higher in the group with WHO shock both in our study (60%, Table 2) and in the FEAST study where it was 20-54% [12] which may suggest that WHO shock is a more severe and possibly late stage of disease.

The low prevalence of WHO shock and the high mortality in children fulfilling the criteria highlight that the definition is too strict to adequately diagnose shock for clinical purposes. Many children who were classified as being shocked in our study, the Kenya study and in the FEAST trial did not fulfill the full WHO criteria yet were included. In our patient group, an admission diagnosis of ‘shock’ was written up for 36/505 (7.1%) of the included cases which is double the figure of 3.4% that we found when we used the four WHO criteria to determine shock. Following the full WHO definition for shock may therefore miss out on some very sick children with severely impaired circulation.

In terms of clinical characteristics, we noted that those who had WHO shock tended to be of a younger age (mean 17 months versus 34 months, p = 0.035), had a higher HIV prevalence (15.3% versus 6.9%, p = 0.001), and were more likely to be malnourished (26.7% versus 6.8%, p=0.022). When it came to presenting complaints, the WHO shock group had less cough and respiratory distress but more vomiting, diarrhoea and difficulties in feeding ($p < 0.05$ for all). The WHO shock group was also more likely to be pale, hypoglycaemic, dehydrated and lethargic with a reduced BCS ($p< 0.002$ for all, Table 2). It is however difficult to draw conclusions from these findings due to the very small sample size of those with WHO shock.

5.4.3 Conclusion on the Definition of Shock

From our findings describing the severely sick patients with WHO shock and also the patients with pure viral/reactive lower respiratory tract disease who may not even have had shock, the spectrum for definition of shock may be too narrow. Using the WHO definition for impaired circulation may thus be a more sensitive way to pick up critically ill children who may not meet the full criteria for the WHO diagnosis of shock. There is an evident lack of a reliable bedside definition of shock/impaired circulation. A wide definition for impaired circulation and a narrow definition of shock produce challenges when it comes to patient management. Having a wide definition for impaired circulation may lead to incorrect administration of fluid boluses to patients who otherwise do not need them, and having a very narrow definition of shock may mean depriving patients who do need fluid boluses from much needed intervention before they reach an irreversible state.

There is need for more thought to be put into the definitions of shock and severely impaired circulation in LMICs like Malawi. Applying a robust definition is essential for clinical and scientific purposes and without this it is impossible to develop evidence based guidelines for shock in children in LMIC. Adaptation of shock definitions and guidelines from high income countries may not have a direct application to our population as LMIC have limited diagnostic and monitoring tools to assess the pre- and post- intervention states of children who come in with a diagnosis of shock.

5.5 Laboratory Markers

Hypoglycaemia is a common complication in critically ill children (25/272 = 9.2%) in our setting. In the SugarFACT study done in Malawi on children who were aged between 1 month and 5 years with either a WHO-defined emergency sign or a clinical concern that the child's condition was an emergency, the incidence of low blood sugar concentration was 451/6706 (6.7%) and that of hypoglycaemia was 1.6% (113/6706) [13]. In our study, only 272/505 (53.9%) of patients had a blood sugar checked. Given the broad definition of shock in our study, some of the children may also have been admitted in the non-resuscitation room where blood sugar is not routinely checked. We found that low blood sugar < 2.4/ 3.0mmol/L or high blood sugar > 10mmol/L was common and significantly associated with mortality (p =0.00, table 5).

Anaemia (Hb <10g/dL) was present in 148/334 (44.3%) but those with severe anaemia (Hb ≤5g/dL) were only 19 (5.7%). This is in stark contrast to the 32% prevalence of severe anaemia found in the multicenter FEAST trial. A possible reason for this may be the higher

proportion of study participants who had malaria in that trial compared to ours (parasitaemia 57% in FEAST trial compared to 17% in our trial).

Blood culture positivity rate was low in our study, and there was no clear association between the diagnosis of sepsis and blood culture positivity. Only 8/176 (4.5%) of blood cultures that were taken in our study grew a significant pathogen yet 12% of our patients had a diagnosis of presumed sepsis. The difference in these figures may either be due to poor blood culture taking techniques, or maybe even a wrong diagnosis where children getting labelled as 'sepsis' may not actually have bacteraemia. Ahmad et al found a blood culture positivity rate in 2004/2005 at QECH paediatric A&E of 93/542 (17%) [7]. This difference, may be explained by the fact that they had a higher prevalence of HIV (152/576 = 26% vs 27/358 =7.5%), malnutrition (60/583 = 10.3% versus 39/471 = 8.3% and a diagnosis of sepsis (218 /583 = 37.4% versus 57/470 = 12.0%) compared to our study population. They may also have had a population of even sicker children which brings bias in the interpretation of blood culture positivity rates.

5.6 Diagnoses

The children in our study with shock commonly had multiple diagnoses (N=190, 40.3%). This may be due to late presentations and severe stages of diseases which are common in our setting. The presence of multiple diagnoses may make the management of children in our setting less straight forward as many factors have to be considered simultaneously when instituting treatment.

The main diagnoses we found were viral/reactive lower respiratory tract disease (44.9%), pneumonia (18.8%), gastroenteritis (13.6%), presumed sepsis (12.0%), malaria (12.0%) and anaemia (6.1%) – Appendix 2. The FEAST trial which assessed a large number of children with severe febrile illness and impaired circulation, found the main diagnoses to be malaria (66%), severe anaemia (43%), lower respiratory tract infection (42%), sepsis (15%), upper respiratory tract infection (11%) and meningitis (3%) [12]. Similar diseases were also found in Kenya by the Clinical Information Network Hospitals who had malaria (40.2%) and pneumonia (46.7%) as top diagnoses [5].

The proportion of children with lower respiratory tract infection of 1345/3141 (43%) in the FEAST trial was very similar to what we found. This may suggest that both in our study and the FEAST trial an important part of the children that were included as being shocked had respiratory distress and tachycardia but may not actually have had shock. It is therefore likely that the symptoms are explained by respiratory distress caused by most likely viral respiratory disease. This is in line with data from rural Kenya in 2007 assessing the aetiologies of pneumonia in children, which showed that in children aged 1 month to 12 years who met the WHO criteria for “severe pneumonia” one or more respiratory viruses were detected in 56% of the participants [14]. Another fact that supports the hypothesis that these children may not have shock or circulatory impairment is the fact that the mortality in this group was 0%, whilst shock even in high resource settings has a mortality up to 10% [2].

Our study found a marked difference in the proportions for the diagnosis of malaria and severe anaemia compared to the FEAST findings and the Kenyan findings. This may be a reflection of a possible difference in malaria prevalence between the countries that participated in the FEAST trial in that time period and the current situation in Malawi.

Gastroenteritis is a significant contributor to morbidity in children from LMICs and 13.6% of our study population had gastroenteritis. Mbevi et al found that 582/622 (93.6%) of all the cases of shock they had were secondary to or complicated by diarrhoea/dehydration [5]. This may have been an overestimate given that their study was done retrospectively from patient diagnoses in hospital charts and there may have been a selection bias in the patients they recruited.

Despite these differences, it seems that shock in low income settings has a more complex etiology with several coinciding conditions. As disease patterns in sub-Saharan Africa countries appear similar, there is need for more collaborative efforts within the region to come up with guidelines and consensuses for management of our very sick children and thus reduce the high mortality.

5.7 Management

There has been growing concern and controversy over the appropriate fluid management for children with circulatory insufficiency after the FEAST trial showed an unexpected increase in 48-hour mortality in severely sick febrile children who received fluid boluses. Current recommendations are for a more careful approach to fluid administration as a part of

resuscitative efforts in children with circulatory insufficiency. For those with shock, an initial fluid bolus of 10-20mls/kg over 30minutes – 1 hour is now recommended, while for those with impaired circulation the recommendation is to avoid giving a fluid bolus but rather give only maintenance fluid [1].

Given the generally low prevalence of WHO shock across studies, there is a concern that may be raised in the fluid management of patients with circulatory insufficiency. Some very ill patients with severely impaired circulation who may not meet all criteria required for fluid bolus therapy according to WHO-shock standards may benefit from fluid bolus therapy. In our study, only 3.4% of participants met the WHO criteria for shock, but fluid boluses were deemed necessary by the admitting clinician and therefore given in 16.4% of patients. The study by Mbevi et al reported that 11% of the children with impaired circulation received fluid boluses [5]. Assuming that clinicians giving care to these children thought it was necessary to give fluids boluses, the question that is then raised is which children within the wide spectrum of circulatory insufficiency could benefit from fluids boluses? The overall population within the FEAST trials, had a poorer outcome with fluid boluses. The study excluded children with gastroenteritis in whom withholding fluids to those who need them may be detrimental. There is therefore a need to investigate shock and severely impaired circulation in children with particular emphasis on definition, which may influence fluid management strategies within the wide spectrum of definitions available.

5.8 Mortality

In our study, we recorded an overall mortality of 11.6%. This is significantly different from what is found in the 6 studies that primarily studied shock where the pooled mortality was 32.8% (95% CI: 16.4-51.6%) [3,5-9]. However, when we split the patient groups, the highest mortality was found in those who had WHO shock (60%, $p < 0.01$) and upon excluding those with primarily respiratory disease (bronchiolitis / viral induced wheeze / asthma), the mortality increased to 26.8% ($p<0.01$). This value is closer to the pooled mortality we found in the 6 studies we reviewed [3, 5-9]. The 26.8% may therefore be a more accurate reflection of the true mortality in patients with shock / severely impaired circulation in our study than the 11.6% that we noted for the whole group. This possibly reflects the effect of the low mortality in the subgroup of viral/reactive lower respiratory tract disease patients.

Our mortality was very similar to the mortality observed in the FEAST study, but they however excluded patients with gastroenteritis and severe malnutrition and therefore their findings may not be directly comparable to ours. Despite this both the overall mortality of 11.6%, and especially the mortality in those without viral / reactive lower respiratory tract disease of 26.8% is much higher than shock outcomes in high income countries where mortality has been reported in 4.5-17% [15-17].

Shock thus has a high mortality with up to one quarter of patients dying at QECH. There is need for more urgent treatment and robust monitoring of such sick patients, with early escalation to high care areas like PICU with more advanced monitoring and treatment options. Due to resource constraints, intensive care may not always be accessible, and even

if it were outcomes may still remain poor given the multiple comorbidities that patients in the LMIC setup exhibit.

5.8.1 Time to Death

We found that 28% of deaths occurred in 24hrs and 55% of deaths had occurred by 48hrs. This is in line with knowledge on critical illnesses in general that suggest that most deaths of children admitted to hospital happen within the first 24 hours of admission [1]. In an audit at Kamuzu Central Hospital it was found that 44% of deaths occurred within the first 24h of admission, and 59% occurred within 48h [18]. Another study done in Kenya comprising a network group of hospitals reported that 57.4% of all deaths in paediatric patients aged 2 months to 15 years at their hospitals had occurred by day 2 of admission [19]. In the FEAST trial 87% of deaths occurred before 24 hours. This highlights a great need to focus on those critical moments when a very sick child arrives to the hospital. WHO recommends that children with severely impaired circulation or shock need to be prioritised for early assessment and treatment and also need to be frequently reassessed [1].

There is also a need for community awareness and education advocating for early presentation to hospital and early referral once a child is sick. From our results we found that the mean duration of symptoms before presenting to hospital ranged between 1.9 – 30 days. This may suggest that there is room to improve on the health seeking behaviour of our patients, or on the referral patterns of our primary health centers which should be encouraged to refer sick patients earlier. Early presentation and referral may reduce mortality.

5.8.2 Predictors of Mortality

Although age group was not found to be independently associated with death in our study (p=0.646), there is still considerable morbidity in younger children. On our multivariate analysis, factors which we found to be associated with death were reduced coma score (BCS ≤4), delayed CRT >3seconds and clinical dehydration (Table 6).

Clinical and laboratory prognostic factors for mortality have previously been analysed in LMIC using the FEAST Paediatric Emergency Triage (PET) score. The score looked at using 8 clinical variables (temperature, heart rate, capillary refill time, conscious level, severe pallor, respiratory distress, lung crepitations, and weak pulse volume) which could be used as prognostic factors to discriminate those at highest risk of fatal outcome at the point of hospital admission. The score ranged from 0–10 and had an AUC-ROC of 0.82 (95 % CI, 0.77–0.87) in the FEAST trial derivation set, and was found to have a discriminative ability which was similar to, or better than other risk scores used in the validation datasets [10]. Our study also found two of the FEAST PET variables to also predict mortality; namely reduced BCS and delayed CRT.

As there is no clear bedside definition of shock, understanding severity using prognostic scores could help to identify those ill children who need urgent critical care. For example, our study had a subset of those with purely reactive / viral lower respiratory tract diseases in whom mortality was 0%, while in the other patients who did not fall into this category the mortality was just over 25%. These patients had differences in symptoms and clinical characteristics that may have been used to identify the children with higher risk for mortality

(Table 3) and thus help to improve classification. Severity signs and prognostic scores may also be helpful in improving treatment guidelines by selecting those that may benefit from a particular treatment and by setting goals to guide treatment. Further analysis of risk factors to mortality and use of prognostic scores in LMICs can help provide rapid bed side clues as to the prognostic risk of patients and therefore may guide in deciding for escalation of care.

5.8.3 Diagnoses and Mortality

The most common diagnoses amongst children that died were presumed sepsis, acute gastroenteritis, malaria, severe malnutrition and meningitis. Presumed sepsis in particular accounted for nearly half of all deaths (44.7%) and was associated with mortality. Sepsis was however diagnosed clinically and only a minority (14.7%) could be confirmed by a positive blood culture (section 5d). The contribution of sepsis may therefore be overestimated as some of these patients could have had an alternate diagnosis.

Despite the fact that this study was not designed to unravel the etiology of shock, a study which is lacking in this context, our findings are in line with other data from similar settings and populations. At Kamuzu Central Hospital in Lilongwe, Malawi, a retrospective death audit was performed analysing mortality data over a 13-month period in the pediatric wards (excluding neonatal wards). They found that some of the most common causes of death were malaria, malnutrition, HIV-related illnesses, sepsis and gastroenteritis [18]. In the FEAST trial most deaths were due to malaria, pneumonia, sepsis, anaemia and meningitis [12].

5.8.4 Mortality Associations

In our explanatory model (Table 7), we found presumed sepsis to be an independent risk factor for mortality, with 63% of those who had a diagnosis of presumed sepsis dying (p =0.007, OR 3.4, 95% CI 1.4 - 8.2). However due to the low blood culture positivity rate we found, the deaths attributed to sepsis may not be entirely accurate as some of these patients may have other diagnoses. Despite these discrepancies, other studies have also found the diagnosis of sepsis to be associated with high mortality. For example, a study in Egypt showed a 24.6% mortality for children admitted to PICU with a diagnosis of sepsis [20] and in Bangladesh, 59/88 (67%) of children under five who were admitted to ICU with a diagnosis of septic shock died [21]. Gastroenteritis was also associated with poor outcome in our patients with 21/53 (39.6%) of those with this diagnosis dying (Table 5). This is comparable to what was found by Mbevi et al where their mortality from diarrhoea and hypovolaemia was 106/326 (33.0%) [5].

HIV was not associated with poor outcome in our study population which is in contrast to the study by Ahmad et al at QECH in children needing resuscitation which showed a link between a positive HIV status and higher mortality [7]. Our findings may be different from this because PMTCT programs and early ART coverage have greatly improved in Malawi since 2004/5 period when the Ahmad study was carried out. As of 2018, more than 95% of pregnant women with HIV accessed antiretroviral medicine, and testing for HIV through early infant diagnosis before 8 weeks of age was more than 95% [22].

Although it seems diseases leading to death in shock are similar in LMICs, there is still need for future aetiological studies on shock assessing the true impact of sepsis and other diseases on mortality in our population of shocked children.

5.9 Shortcomings

Full classification of all patients to determine the prevalence of severely impaired circulation / WHO shock was not possible in our study because of some missing data due to lack of documentation of all clinical features by admitting teams. This may have led to some bias, and some patients who may have fit into these categories may very well have been left out. It is therefore difficult to accurately determine which clinical features, diagnoses, and laboratory markers are associated with shock / severely impaired circulation. Inadequate documentation is not a new phenomenon in hospitals in Malawi and other regions, and this is supported by a 2018 death audit done by Fitzgerald et al at Kamuzu Central Hospital where they also noted inadequate record keeping and sections of vital data missing from the hospital records in critically ill children [18]. This can be a learning point for the major referral hospitals in Malawi to encourage improved documentation of vital patient information. Despite these flaws, we presented the first prospective data on prevalence of shock in an African paediatric population.

Another shortcoming was that we did not manage to consent and recruit 25% of all eligible patients, mainly because they were discharged before consenting, with few of them declining consent. As being discharged before consenting occurred more often in the shorter admissions, this may mean that they had different diseases that could have led to quicker

recovery than other diseases associated with shock, and may be another source of bias in our study.

We also applied a broad definition of shock to perform an inclusive study, however this overestimated the prevalence of shock and has thus affected the overall clinical characteristics and aetiological diseases of the children in shock. We however tried to account for this by making sub analysis of the different patient groups in order to get a more accurate picture.

The determination of aetiology was based on clinical diagnoses supported by laboratory testing. Ideally a detailed study would test for all potential causes and thus may more accurately reflect the real diagnoses.

CHAPTER SIX: CONCLUSION

Shock is a relatively common diagnosis in paediatric patients at QECH, and may affect up to 5% of all children admitted. WHO shock criteria was not well defined since it was found in about 3% of study participants (0.1% of all admissions). Therefore, the above findings underline the need for a reliable bed-side definition of shock that can be used in LMIC.

Shock causes significant mortality in children, accounting for up to 12% of our total study participants and 25% of those with the stricter shock definition that excluded viral / reactive lower respiratory tract diseases dying. Children under 5 years of age are more severely affected. Predictors of poor outcome included reduced coma score and delayed capillary refill time (> 3 sec).

There is a wide spectrum of diseases that can lead to shock, with sepsis, gastroenteritis and malaria being significant contributors to mortality in very sick children. It is therefore recommended that a detailed etiological study be undertaken in order to shed more light on the subject and potentially improve outcomes.

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APPENDICES

Appendix 1: Case Record Form

Eligibility form

CISSAC AUDIT&PILOT Once completed keep separate from rest of CRF

SCREENING NUMBER: Screen - _ _ _ _ _

DATE IN A&E: _ _ / _ _ / 20_ _ **TIME IN A&E** _ _ : _ _

DATE SCREENED _ _ / _ _ / 20_ _

ADMITTED ☐YES ☐NO ☐UNKOWN

TO WARD ☐PSCW ☐PICU ☐OTHER:_____

STILL ADMITTED ☐YES ☐NO ☐UNKOWN

INCLUSION CRITERIA & CONSENT

A. One or both of:

- ☐ **impaired consciousness (prostration or coma),**
- ☐ **respiratory distress (increased work of breathing),**

B. AND at least one sign of impaired perfusion:

- ☐ **capillary refill time>3 seconds,**
- ☐ **lower-limb-temperature gradient,**
- ☐ **weak radial-pulse volume,**
- ☐ **severe tachycardia (>180bpm if<12 months, >160bpm 1-5 years, >140bpm >5 years)**

C. AUDIT consent: ☐GIVEN ☐ REFUSED ☐ DISCHARGED/DIED

FORM COMPLETED: ☐YES ☐ NO ☐ NOT POSSIBLE

D. **PILOT consent:** ☐GIVEN ☐ REFUSED ☐ DISCHARGED/DIED

FORM COMPLETED: ☐YES ☐ NO ☐ NOT POSSIBLE

COMPLETE SECTION ONLY IF PATIENT CAN BE INCLUDED AND CONSENT GIVEN

STUDY NUMBER: **AUDIT -** _ _ _ _ **PILOT-** _ _ _ **HOSPITAL NUMBER:** _ _ _ _ _ _

FIRST NAME: _

LAST NAME: _

Date of Birth : _ _ / _ _ / 20_ _ **OR** **AGE:** _ _ months & _ _years **OR** ☐Unknown

SEX: ☐Male ☐Female ☐ Not Documented

Appendix 2: Case Record Form

Study number Audit - _ _ _ _ Completed by _ _

CRF – CISSAC AUDIT

Date of admission: _ _ / _ _ / 20_ _ **Time of admission:** _ _ : _ _

Date of data collection: _ _ / _ _ / 20_ _

DEMOGRAPHICS (circle the correct one)

Date of Birth : _ _ / _ _ / 20_ _ **OR AGE:** _ _ months & _ _years **OR** ☐ Unknown

SEX: ☐ Male ☐ Female ☐ Not Documented

HIV STATUS: ☐ Reactive ☐ Non-Reactive ☐ Exposed ☐ Unknown

HISTORY (tick the appropriate box)

	YES	NO	Not Documented	Duration (if yes)
FEVER				
CONVULSIONS				
DIARRHOEA				
VOMMITING				
COUGH				
DIFFICULTY BREATHING				
RASH				
PALLOR				
JAUNDICE				
OEDEMA				
PROBLEMS URINATING				
PROBLEMS FEEDING				
TRAUMA				
If yes describe				
OTHER				
If yes describe				

pg. 1 CASE RECORD FORM CISSAC AUDIT

Appendix 3: Case Record Form

Study number Audit - _ _ _ _ Completed by _ _

CLINICAL FEATURES

Weight:	_ _ . _ **kg**	**OR**	☐ Not Documented
MUAC:	_ _ . _ **cm**	**OR**	☐ Not Documented
Temperature	_ _ . _ **°C**	**OR**	☐ Not Documented
Pulse rate	_ _ _ **/min**	**OR**	☐ Not Documented
Capillary Refill time	_ _ **seconds**	**OR**	☐ Not Documented
Respiratory Rate	_ _ _ **/min**	**OR**	☐ Not Documented
Blantyre Coma Score	_ **/5**	**OR**	☐ Not Documented
Nutrition:	☐ Good ☐ Fair ☐ Poor		☐ Not Documented

(Tick appropriate)	YES	NO	Not Documented
Pallor			
Jaundice			
Oedema			
Rash			
Dehydration			
Finger Clubbing			
Lymphadenopathy			
Oral thrush			
Respiratory Distress			
Heart Murmur			
Hepatomegaly			
Splenomegaly			
Lethargy			
Neck Stiffness			
Ear Discharge			
Cold peripheries			

ADMISSION DIAGNOSIS

1. _____
2. _____
3. _____

Appendix 4: Case Record Form

Study number Audit - _ _ _ _ Completed by _ _

CLINICAL MANAGEMENT IN A&E

	YES	NO	If yes, specify TYPE	Total Amount
Bolus Fluids			☐ Ringers Lactate ☐ Normal Saline ☐ Other (specify)	_ _ _ mls/kg _ _ _ mls/kg _ _ _ mls/kg
Blood product transfusion			☐ Whole blood ☐ Packed red cells ☐ Fresh Frozen Plasma ☐ Platelets	_ _ _ mls/kg _ _ _ mls/kg _ _ _ mls/kg _ _ _ mls/kg
Antibiotics			☐ Crystalline penicillin ☐ Gentamycin ☐ Ceftriaxone ☐ Ciprofloxacin ☐ Other (specify) _____	
Antimalarials			☐ Artesunate ☐ Lumefantrine Artemether	

Intraosseous Line inserted? ☐YES ☐NO ☐Not Documented

CPR done in A&E? ☐YES ☐NO ☐Not Documented

Adrenaline Given in A&E ☐YES ☐NO ☐Not Documented

LABORATORY RESULTS IN A&E

1. **First Random Blood Sugar:** _ _ _ mg/dL **OR** ☐Not Documented/Done
   _ _ . _ mmol/L
2. **Packed Cell Volume:** _ _ % **OR** ☐Not Documented/Done
3. **Haemoglobin:** _ _ . _ **g/dL** **OR** ☐Not Documented/Done
4. **Malaria Blood Film:** ☐Positive ☐Negative ☐Not Documented/Done
5. **MRDT** ☐Positive ☐Negative ☐Not Documented/Done
6. **Blood Culture** ☐Positive ☐No Growth/contaminant ☐Not Done
   ↳ specify organism:_____

Appendix 5: Case Record Form

Study number Audit - _ _ _ _ Completed by _ _

BACKGROUND & OUTCOME

Vaccination status: Complete Incomplete Not Documented

Previous Admission: ☐ Yes ☐ No ☐ Not Documented

Number of admissions: _ _
Any with shock: ☐ Yes ☐ No ☐ Unknown

Past Medical History

Pre – Exisiting Chronic Conditions	YES	NO	Not Documented	(if YES, please specify)
Cardiac disease				
Respiratory disease				
Neurological condition				
Haematological condition				
Gastrointestinal condition				
Renal disease				
Malignancy				
Malnutrition/failure to thrive				
Rheumatologic condition				
Other (specify)				

OUTCOME

☐ DISCHARGED ALIVE Date of discharge: _ _ / _ _ / 20_ _

☐ ABSCONDED Date last seen: _ _ / _ _ / 20_ _

☐ NOT DOCUMENTED Date last seen: _ _ / _ _ / 20_ _

☐ DEAD Date of death: _ _ / _ _ / 20_ _ Time of death: _ _ : _ _

☐ Died in A&E ☐ Died in ward ☐ Elsewhere:_____

DISCHARGE / DEATH DIAGNOSIS

1. _____
2. _____

pg. 4 CASE RECORD FORM CISSAC AUDIT

Appendix 6: Patient Diagnoses

DIAGNOSIS	COUNT (N=505)	PERCENTAGE
Bronchiolitis	120	24.8%
Severe pneumonia	89	18.4%
Viral induced wheeze	62	12.8%
Severe malaria	57	11.8%
Presumed Sepsis	57	11.8%
Acute gastroenteritis	35	7.2%
Acute gastroenteritis with severe dehydration	29	6.0%
Anaemia	29	6.0%
Acute asthmatic attack	29	6.0%
Severe malnutrition	21	4.3%
Meningitis	15	3.1%
Tuberculosis	12	2.5%
Cerebral malaria	10	2.1%
Congenital heart disease	10	2.1%
Encephalitis	8	1.7%
Rheumatic heart disease	7	1.4%
Hypoglycemia	5	1.0%
Congestive heart failure	5	1.0%
Febrile convulsions	4	0.8%
Cerebral palsy	4	0.8%
Glomerulonephritis	3	0.6%
Congenital Anomalies	3	0.6%
Diabetic ketoacidosis	3	0.6%
Croup	3	0.6%
Empyema	3	0.6%
Epilepsy	3	0.6%
Poisoning	2	0.4%
Acute kidney injury	2	0.4%
Severe dehydration	2	0.4%
Chronic gastroenteritis	2	0.4%
Acute liver failure	2	0.4%
Typhoid	2	0.4%
Moderate malnutrition	2	0.4%
Kaposi sarcoma	2	0.4%
Sickle cell disease	2	0.4%
***Pneumocystis Jiroveci* pneumonia**	2	0.4%
Upper respiratory tract infection	2	0.4%
Brain tumour	2	0.4%
Disseminated *Staphylococcal* infection	2	0.4%

Appendix 7: Patient Diagnoses

DIAGNOSIS	COUNT (N=505)	PERCENTAGE
Malignancy	2	0.4%
Dilated cardiomyopathy	2	0.4%
Acute rheumatic fever	2	0.4%
Cardiogenic shock	2	0.4%
Myocarditis	2	0.4%
Inguinal hernia	1	0.2%
Head injury	1	0.2%
Nephrotic syndrome	1	0.2%
Laryngomalacia	1	0.2%
Acute abdomen / Peritonitis	1	0.2%
Bowel obstruction	1	0.2%
Cleft lip / palate	1	0.2%
Drowning	1	0.2%
Intraabdominal trauma / visceral bleed	1	0.2%
Recurrent laryngeal papillomas	1	0.2%
Malrotation	1	0.2%
Cystic fibrosis	1	0.2%
Diaphragmatic paralysis	1	0.2%
Oesophageal candidiasis	1	0.2%
Paralytic ileus	1	0.2%
Hypertension	1	0.2%
Posterior urethral valves	1	0.2%
Disseminated intravascular coagulation	1	0.2%
Gastrointestinal bleeding	1	0.2%
Gastritis	1	0.2%
Hepatic cyst	1	0.2%
Acute chest syndrome	1	0.2%
Chronic lung disease	1	0.2%
Pleural effusion	1	0.2%
Pertussis	1	0.2%
Pneumothorax	1	0.2%
Rabies	1	0.2%
Encephalopathy	1	0.2%
Space occupying lesion	1	0.2%
Hydrocephalus	1	0.2%
Todd's palsy	1	0.2%
Microcephaly	1	0.2%
Abscess	1	0.2%
Chronic otitis media	1	0.2%
Bullous impetigo	1	0.2%
Scabies	1	0.2%
Urinary tract Infection	1	0.2%
Chickenpox	1	0.2%
Presumed severe HIV disease	1	0.2%
Atrial fibrillation	1	0.2%