



RESEARCH ARTICLE

REVISED Mortality during and following hospital admission among school-aged children: a cohort study [version 2; peer review: 3 approved]

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Abstract

Background: Far less is known about the reasons for hospitalization or mortality during and after hospitalization among school-aged children than among under-fives in low- and middle-income countries. This study aimed to describe common types of illness causing hospitalisation; inpatient mortality and post-discharge mortality among school-age children at Kilifi County Hospital (KCH), Kenya.

Methods: A retrospective cohort study of children 5–12 years old admitted at KCH, 2007 to 2016, and resident within the Kilifi Health Demographic Surveillance System (KHDSS). Children discharged alive were followed up for one year by quarterly census. Outcomes were inpatient and one-year post-discharge mortality.

Results: We included 3,907 admissions among 3,196 children with a median age of 7 years 8 months (IQR 74–116 months). Severe anaemia (792, 20%), malaria (749, 19%), sickle cell disease (408, 10%), trauma (408, 10%), and severe pneumonia (340, 8.7%) were the commonest reasons for admission. Comorbidities included 623 (16%) with severe wasting, 386 (10%) with severe stunting, 90 (2.3%) with oedematous malnutrition and 194 (5.0%) with HIV infection. 132 (3.4%) children died during hospitalisation. Inpatient death was associated with signs of disease severity, age, bacteraemia, HIV infection and severe stunting. After discharge, 89/2,997 (3.0%) children died within one year during 2,853 child-years observed (31.2 deaths [95%CI, 25.3–38.4] per 1,000 child-years). 63/89 (71%) of post-discharge

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deaths occurred within three months and 45% of deaths occurred outside hospital. Post-discharge mortality was positively associated with weak pulse, tachypnoea, severe anaemia, HIV infection and severe wasting and negatively associated with malaria.

Conclusions: Reasons for admissions are markedly different from those reported in under-fives. There was significant post-discharge mortality, suggesting hospitalisation is a marker of risk in this population. Our findings inform guideline development to include risk stratification, targeted post-discharge care and facilitate access to healthcare to improve survival in the early months post-discharge in school-aged children.

Keywords

Mortality, Inpatient, Post-discharge, Reason for admission, School-aged children, Cohort, Africa



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REVISED Amendments from Version 1

Introduction, clarified on paragraph three: two studies referenced in the background used same participants from Tanzania to evaluate effect of admission diagnosis and levels of hemoglobin on post-discharge mortality respectively.

Methods, Study settings: Paragraph 1 and 2; Added details of the common admission diagnosis for children 1 to 59 admitted at KCH. Provided more details of enumeration in the KHDSS and measures for improving data quality.

Statistical methods: Explained how anthropometric measurements and systematically collected laboratory tests missing values were handled in the analysis and referenced a new table (Extended data Table S1) with list of variables missing data.

Results, Post-discharge mortality: Paragraph 1; Provided a summary of where the 89 post-discharge deaths occurred and causes of deaths for 26 deaths that occurred during readmission at KCH (Extended data Table S6, new table added).

Paragraph 2; Provided results of proportion of children who absconded from hospital.

Replaced [Figure 2](#) with a new one that includes 95% confidence intervals.

Discussion, Paragraph 1: explained the results on association of epilepsy/convulsion with inpatient mortality.

Paragraph 2: Explained the post-discharge mortality rate in reference to background mortality within KHDSS and causes of deaths estimated from verbal autopsies in KHDSS.

Last paragraph: Added unavailable causes of deaths among those children who died in community or other health facilities as a study limitation.

Any further responses from the reviewers can be found at the end of the article

Introduction

Despite a remarkable decline in global child mortality, more than 6 million children died in 2018, of which 0.9 million (15%) deaths occurred among children aged 5 to 14 years, mostly in low- and middle-income countries (LMICs)^{1,2}. Public health efforts to improve survival are generally directed towards children <5 years old²⁻⁴. Despite there being no specific new health interventions targeting children aged 5 to 14 years, their mortality risk from 1990 to 2016 declined by 51% globally⁴. However, since 2000, the annual rate of mortality reduction in this group (2.7%) has been lower than amongst children <5 years old (4.0%)⁴.

Children ≥5 years old may be admitted to hospital with different conditions than younger children and their risks for inpatient or post-discharge mortality may also differ. However, there are only limited data describing reasons for admission and mortality-patterns in LMICs. Among school-aged children admitted to six Kenyan hospitals in 2013, 3.5% of children aged 5 to 9 years and 5.0% of children 10 to 14 years died⁵. Infectious diseases such as malaria were the main reported causes of death in children ≥5 years^{2,5,6}.

Post-discharge mortality is increasingly recognized as a significant contributor to the burden of mortality among under-fives in

LMICs and adults in resource-rich settings⁷⁻⁹. The most recent systematic review (2018) of paediatric post-discharge mortality in LMICs did not identify any studies focusing specifically on school-aged children^{7,8}. Of 24 studies reviewed, four included children ≥5 years old. A study in Bangladesh with a sample size of 74 children aged 24 to 72 months did not report the number of children who were ≥5 years old¹⁰. A large study in Kenya among children 0 to 15 years old (N=14,971) reported that 16% (88/535) of all post-hospital discharge deaths were among children aged 5 to 14 years¹¹ and two studies from Uganda with children aged 2 months to 12 years reported ~1% and 3.8% children dying after discharge, respectively, but were not disaggregated by age group^{12,13}. Since the latest systematic review (2018)⁷, four more studies have evaluated paediatric post-discharge mortality in LMICs^{3,14-16}. Hau *et al.* included children aged 2 to 12 years followed-up for 12 months after discharge from two hospitals in Tanzania and found that 16% (26/161) of children aged 5 to 12 years died after hospital discharge³. Post-discharge mortality risk was reported to be higher than that of children <5 years (hazard ratio 2.44 (95%CI, 1.37 to 4.34)³. The commonest diagnoses at admission were malaria and sickle cell disease³. The second study from southern Mozambique included 18,023 children aged <15 years, of which 83/3,816 (2.2%) aged ≥5 years died within three months after discharge¹⁴. The third study was from Kenya, but excluded children ≥5 years old¹⁵. The fourth study from Tanzania included children aged 2 to 12 years, of whom 47/466 (10%) died one year after hospital discharge, but deaths were not disaggregated by age¹⁶. Two of the four studies from Tanzania, used same study participants to evaluate overall one-year post-discharge mortality based on admission diagnosis³ and on levels of haemoglobin¹⁶ respectively.

In this retrospective cohort study, we aimed to describe the reasons for hospitalisation, underlying illnesses, and the clinical characteristics and features associated with mortality during hospitalisation and for one year after discharge among children 5 to 12 years old admitted to a rural hospital in Kenya.

Methods

Study setting

The study was conducted at Kilifi County Hospital (KCH), located on the Indian Ocean coast in Kenya. KCH is a secondary care hospital handling approximately 5,000 annual paediatric admissions. At KCH, approximately 60% of paediatric admissions are aged 1 to 59 months, who are mostly admitted and treated for pneumonia and diarrhoea^{15,17,18}. Most of the population served by the hospital are rural farmers. Clinical care at the hospital follows Kenyan and World Health Organization (WHO) guidelines.

Systematic data including clinical signs, anthropometry and laboratory investigations at admission have been collected by research clinicians and entered in a database since 1998. At discharge or death, up to two final diagnoses are assigned by the discharging clinician. From 2002, approximately 250,000 residents in an area of 891 km² neighbouring KCH have been enumerated every four months by the Kilifi Health and Demographic Surveillance System (KHDSS) for births, deaths

and in- or out-migration¹⁹. During each enumeration round, data collectors move from one household to another using GIS-derived maps and ask pre-specified questions to the head of household and other members as described elsewhere¹⁹. Data on admissions to KCH are linked to the KHDSS population database by matching individual child using unique ID number through pre-designed database query programme. Both the KCH admissions and KHDSS databases are programmed with validation checks to improve data quality. Community enumerators within the KHDSS, clinicians and clinical assistants collecting data in the KHDSS and KCH respectively are regularly trained.

Study population

Children aged 60 to 155 months admitted to KCH between 2007 and 2016 and resident within the KHDSS were included. The post-discharge analysis included all children discharged alive. Data from the KHDSS up to the 2018 August census round were used to confirm vital status post-discharge.

Study design

We performed a retrospective cohort study. Exposures evaluated were clinical and demographic features, anthropometry and laboratory variables at admission. Outcomes examined were inpatient and one-year post-discharge mortality.

Data sources/measurement

Anthropometry, clinical history and examination, complete blood count, HIV antibody test, blood smear for malaria and blood culture were systematically conducted at admission as previously described²⁰. Anthropometry was taken by trained clinical assistants: mid-upper arm circumference (MUAC) using a non-stretchable insertion tape (TALC, St Albans, UK), weight using an electronic scale (Seca 825, Birmingham, UK) and height using a stadiometer (Seca 215, Birmingham, UK) which were regularly checked for consistency. HIV antibody testing used two rapid tests (Determine; Inverness Medical, FL, USA; and Unigold; Trinity Biotech, Bray, Ireland). Caregivers of children with a positive HIV antibody test were counselled and referred to an HIV comprehensive care clinic. Details of subsequent outpatient clinic attendance and antiretroviral treatment were not recorded on the database. Children found to have malnutrition, sickle cell disease, tuberculosis, cardiac or neurological conditions were referred to outpatient clinics for continued care.

For this analysis, malaria was defined as a blood smear positive for *Plasmodium falciparum* and anaemia was defined as moderate (haemoglobin 8 to 11.4 g/dl) or severe (haemoglobin <8g/dl), as per WHO guidelines²¹. Biochemical tests, radiology, sickle cell testing, lumbar puncture and other investigations were done at the discretion of the treating clinician. Meningitis was diagnosed using the cerebrospinal fluid (CSF) examination and culture as follows: positive culture for known pathogen, positive CSF microscopy (Gram stain and/or Indian ink stain), positive antigen test (*S. pneumoniae*, *H. influenzae* type B, *N. meningitidis*, and *C. neoformans*) and CSF white blood cell count (WBC) ≥ 10 cells/ μ l.

Statistical methods

Statistical analysis was performed using STATA (version 15.1; StataCorp, College Station, TX, USA). All eligible admissions and discharges from the population of KCH residents of KHDSS within the study period were included in the study, therefore, no formal sample size estimation was conducted.

MUAC-for-age z-score (MUACZ) were calculated using the method of Mramba *et al.*²². Body mass index-for-age z-score (BMIZ), weight-for-age (WAZ) and height-for-age z-score (HAZ) were calculated using WHO 2007 growth references and classified as normal ($\geq 2Z$), moderate (-3 to $-2Z$) and severe ($< -3Z$)²³. Anthropometric measurements and systematically collected laboratory tests were regarded as missing not at random (*Extended data* Table S1). To ensure all children were included in the multivariable regression models, we used categorical variables and included a 'missing' category in the analysis.

Because the children could be admitted more than once during the study period, for the analysis of inpatient deaths we performed a multiple-admission analysis where each child could contribute more than one admission record using their unique person IDs. To examine features at admission associated with inpatient mortality, we used a backward stepwise log-binomial regression model with robust standard errors to account for multiple admissions retaining variables with a P-value < 0.1 and reported adjusted risk ratios for variables with P-value < 0.05 in the final multivariable model.

To calculate the post-discharge mortality rate, time at risk was defined as the date of hospital discharge until death, out-migration or 365 days later. We performed a multiple-discharge analysis where children with multiple admissions with live discharge contributed separate person-time periods when there was no overlap during the one-year follow-up. After assessing and confirming the proportional hazard assumption was not violated using the Schoenfeld residuals test, we used a Cox proportional hazard regression model with robust standard errors to account for multiple discharges to examine admission features associated with post-discharge mortality.

For both inpatient and post-discharge regression analysis, individual clinical signs, laboratory tests and final diagnoses assigned by clinical staff were used for diagnoses not captured by syndromic definitions using clinical signs. In the regression models, we used MUACZ to define undernutrition rather than BMIZ because MUACZ predicts mortality as effectively as BMIZ²², is less affected by dehydration than weight-based measures²⁴, and fewer children were missing MUAC measurements. We initially excluded biochemical features that were not systematically collected and performed exploratory analyses of these features. We tested if the effects of HIV status, anaemia and malaria were modified by age and if the malaria effects on post-discharge mortality were modified by anaemia or nutritional status using likelihood-ratio tests. Goodness-of-fit of the

multivariable regression models was assessed using the area under receiver operating characteristic curves (AUC) and internally validated using the bootstrapping method with 1000 resampling with replacement²⁵.

Ethical statement

The Kenya Medical Research Institute (KEMRI) National Ethics Review Committee (SCC 2778) approved the study. Written consent for the children's participation in the original study was provided by their parents/guardians, which included consent for subsequent analyses.

Results

From 2007 to 2016, there were 41,107 paediatric admissions to KCH, of which 7,063 (17%) were aged 5 to 12 years (Figure 1). Of these, 3,907 (55%) admissions among 3,196 children were KHDSS residents and were included in this analysis (Figure 1). Their median age was 92 (IQR 74–116) months and 1,673 (43%) were female. Of the 3,907 admissions, 792 (20%) presented with severe anaemia, 749 (19%) with

malaria, 408 (10%) with sickle cell disease (known at admission or diagnosed during admission), 408 (10%) had suffered trauma, 340 (8.7%) with severe pneumonia and 194 (5.0%) with diarrhoea.

Underlying chronic conditions included stunting in 1,143 (29%), severe stunting in 90 (2.3%), severe wasting (MUACZ <-3) in 623 (16%), HIV infection in 194 (5.0%), and nutritional oedema in 90 (2.3%) (Table 1, Table 2 and Extended data Table S2).

A total of 138 (3.5%) children had detectable bacteraemia (Table 1). The commonest bacteria isolated were: *Streptococcus pneumoniae* (47/138, 34%), *Staphylococcus aureus* (32/138, 23%) and non-typhi *Salmonella species* (21/138, 15%) (Extended data Table S3). The final diagnoses assigned by clinicians are shown in Table 2.

There were 132 (3.4%) inpatient deaths. The median (IQR) time to inpatient death was one (1–4) days, while median (IQR)

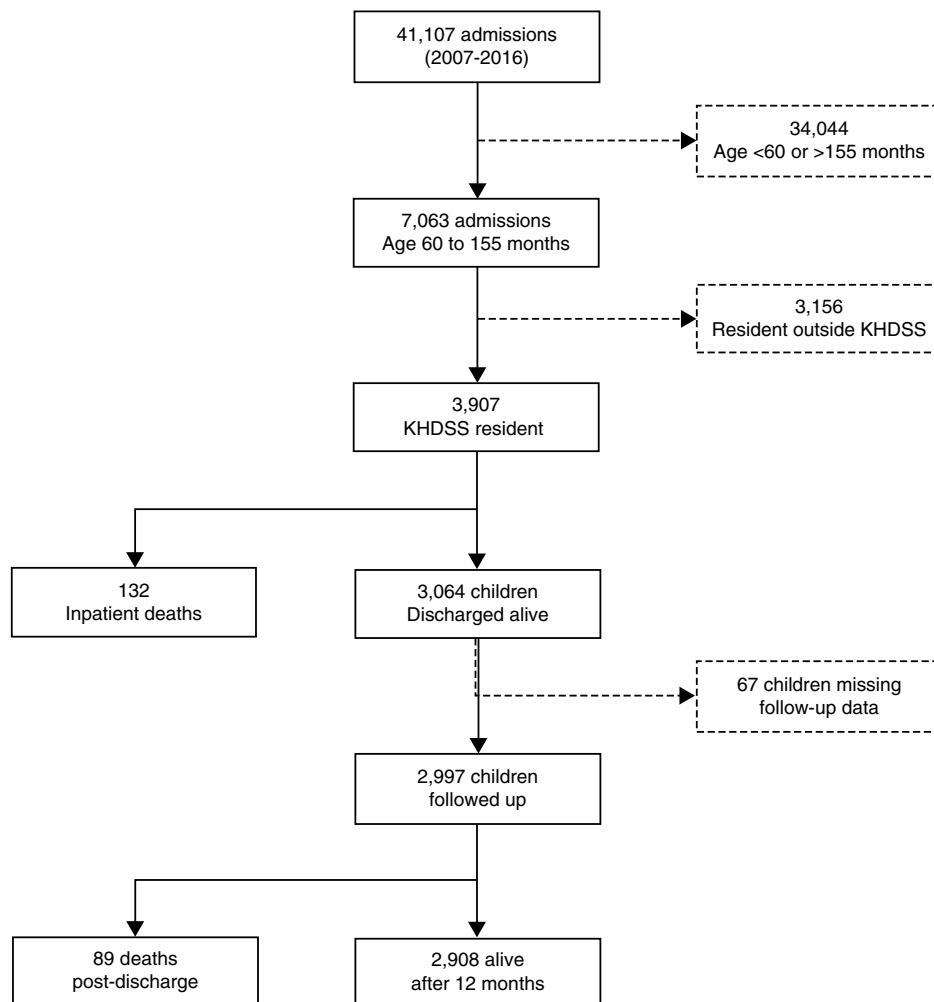


Figure 1. Study participant recruitment and follow-up. KHDSS, Kilifi Health Demographic Surveillance System.

Table 1. Participants' characteristics at admission to hospital.

Admission characteristics (N=3,907)	No. (%)
Demographics	
Age in months, median (IQR)	92 (74–116)
Sex (female)	1673 (43)
Had been admitted prior to age 5 years, before this study	1152 (29)
Clinical features	
Axillary temp <36°C	238 (6.1)
Axillary temp 36 to 37.5°C	2009 (51)
Axillary temp >37.5°C	1660 (43)
Respiratory rate <20 breaths per min	80 (2.1)
Normal respiratory rate	2179 (56)
Respiratory rate >30 breaths per min	1580 (40)
Subcostal indrawing	249 (6.4)
History of breathing difficulty	432 (11)
Hypoxia (SaO ₂ <90%)	130 (3.3)
Heart rate <80 beats per min	156 (4.0)
Normal heart rate	1694 (43)
Heart rate >120 beats per min	2035 (52)
Capillary refill >2 seconds	98 (2.5)
Temperature gradient	152 (3.9)
Weak pulse	85 (2.2)
Lethargy	417 (11)
Sunken eyes	132 (3.4)
Reduced skin turgor	71 (1.8)
Impaired consciousness*	540 (14)
Severe pneumonia	340 (8.7)
Diarrhoea	194 (5.0)
Nutritional status	
Nutritional oedema	90 (2.3)
MUAC-for-age z-score (sd)	-1.89 (1.5)
BMI-for-age z-score (sd)	-1.37 (1.2)
Height-for-age z-score (sd)	-1.46 (1.3)
Weight-for-age z-score (sd)	-1.81 (1.2)
Laboratory investigations	
HIV infected	194 (5.0)
Malaria smear positive	749 (19)

Admission characteristics (N=3,907)	No. (%)
Anaemia	
None (haemoglobin ≥11.5g/dl)	817 (21)
Moderate (haemoglobin 8 to 11.4g/dl)	1497 (38)
Severe (haemoglobin <8g/dl)	792 (20)
Bacteraemia	
Meningitis	54 (1.4)

*Defined as presence of prostration or coma. MUAC, mid-upper arm circumference; BMI, body mass index; sd, standard deviation. 49 (1.3%) records missing MUAC, 442 (11%) records missing BMI, 287 (7.3%) records missing height-for-age z-score, 881 (23%) records missing weight-for-age z-score, 22 (0.6%) records missing heart rate, 68 (1.7%) records missing respiratory rate.

time to discharge among the survivors was three (2–6) days. There were 44 (5.6%), 30 (4.0%), 45 (13%), 23 (17%), 9 (17%), and 10 (5.2%) deaths among those admitted with severe anaemia, malaria, severe pneumonia, bacteraemia, meningitis and diarrhoea, respectively. There were 21 (11%), 34 (5.5%), 10 (2.5%) and 4 (1.2%) deaths among children who were HIV-infected, severely wasted, had sickle cell disease and Epilepsy/convulsion, respectively (Table 2 and Extended data Table S2).

Factors associated with inpatient mortality

In the multivariable model, older age, signs of disease severity (tachypnoea, history of breathing difficulty, weak pulse and impaired consciousness), HIV infection, bacteraemia and severe stunting were positively associated with inpatient mortality, whilst epilepsy/convulsions were negatively associated with inpatient mortality (Table 3). All variables tested in univariable analysis are shown in Extended data Table S4. Being severely wasted was associated with inpatient death in the univariable model, but the effect was attenuated in the multivariable model (Extended data Table S4). There was no evidence that the effect of HIV infection on inpatient mortality was modified by age (P=0.13), severe wasting (P=0.97), malaria (P=0.34) or moderate and severe anaemia (P=0.13). We found no evidence that anaemia (P=0.16), age (P=0.21) or severe wasting (P=0.14) modified the effect of malaria on inpatient mortality.

In exploratory analysis including biochemical variables, hyperkalaemia and elevated creatinine were associated with inpatient mortality (Extended data Table S5).

Post-discharge mortality

Among the 3,064 children who were discharged alive, follow-up data were missing for 67 (2.2%) children (Figure 1). We therefore analysed data from 2,997 children who accrued 2,853 child-years of observation. Eighty-nine (3.0%) children died during follow-up; 63 (71%), 80 (90%) and 84 (94%) of post-discharge deaths occurred within three, six and nine months of discharge, respectively. The overall mortality rate was 31.2 (95%CI, 25.3 to 38.4) per 1,000 child-years. During the first three, six and nine months after discharge, mortality rate was

Table 2. Diagnoses assigned at discharge or death.

Discharge diagnosis (N=3,907)	No. (%) Diagnosis one*		No. (%) Diagnosis two*	
	All admissions (N=3,907)	Inpatient Deaths (N=132)	All admissions (N=3,907)	Inpatient Deaths (N=132)
Malaria	793 (20)	32 (4.0)	41 (1.1)	4 (9.8)
Sickle cell disease	408 (10)	10 (2.5)	94 (2.4)	5 (5.3)
Trauma/fractures/accidents	408 (10)	6 (1.5)	23 (0.6)	1 (4.3)
Anaemia	234 (6.0)	9 (3.8)	254 (6.5)	14 (5.5)
Epilepsy/convulsions	198 (5.1)	2 (1.0)	148 (3.8)	2 (1.4)
Lower respiratory tract infection	196 (5.0)	5 (2.6)	76 (2.0)	2 (2.6)
Snake bite	179 (4.6)	0	1 (0.03)	0
Cellulitis/pyomyositis	110 (2.8)	0	24 (0.6)	0
Gastroenteritis	110 (2.8)	0	28 (0.7)	1 (3.6)
Upper respiratory tract infection	76 (2.0)	0	38 (1.0)	0
Burns	75 (1.9)	1 (1.3)	2 (0.05)	0
Elective surgery	75 (1.9)	0	9 (0.2)	0
Malnutrition	73 (1.9)	1 (1.4)	34 (0.9)	5 (15)
Acute abdomen	69 (1.8)	3 (4.3)	4 (0.1)	0
Immunosuppression	53 (1.4)	8 (15)	114 (2.9)	12 (11)
Meningitis	48 (1.2)	12 (25)	6 (0.2)	1 (17)
Diabetes	44 (1.1)	0	3 (0.08)	0
Encephalopathy	44 (1.1)	5 (11)	11 (0.3)	3 (27)
Others	649 (17) [†]	38 (5.9) [‡]	225 (5.8) [¶]	18 (8.0) [#]
None specified	65 (1.7)	0	2,775 (71)	65 (2.3)

*Clinicians assign up to two diagnoses at death or discharge.

[†]Cholera-12, rabies-9, measles-10, tetanus-15, osteomyelitis-20, asthma-44, empyema-3, pleural effusion-3, nephrotic syndrome-52, cerebral palsy-14, pyogenic arthritis-9, congenital disease-32, encephalopathy-44, hydrocephalus-5, acute flaccid paralysis-5, skin disease-19, arthritis-25, poisoning-43, unclassified disease-142, Burkitt's lymphoma-2, dental-3, septicaemia-37, viral infection-14, urinary tract infection-22, viral hepatitis-25, pulmonary tuberculosis-20, otitis media-4, chickenpox-6, genital problems-5, conjunctivitis-5.

[‡]Immunosuppression-8, septicaemia-6, pulmonary tuberculosis-5, rabies-5, tetanus-3, heart disease-6, cerebral palsy-1, hydrocephalus-1, Burkitt's lymphoma-1, viral hepatitis-1, chickenpox-1.

[¶]Cholera-4, tetanus-3, osteomyelitis-3, asthma-15, empyema-3, pleural effusion-4, nephrotic syndrome-15, cerebral palsy-16, chromosomal abnormality-2, heart disease-13, developmental delay-5, skin disease-12, poisoning-3, unclassified disease-20, septicaemia-34, conjunctivitis-6, urinary tract infection-18, renal failure-14, viral hepatitis-8, pulmonary tuberculosis-16, otitis media-6, chickenpox-3, genital problems-2, no second diagnosis-2775.

[#]Empyema-1, cerebral palsy-1, chromosomal abnormality-1, unclassified disease-3, septicaemia-7, renal failure-3, pulmonary tuberculosis-1, chickenpox-1.

244 (95%CI, 190.3 to 311.8), 89.6 (95%CI, 72.0 to 111.6), and 53.2 (95%CI, 43.0 to 65.9) per 1000 child-years, respectively. Forty (45%) deaths occurred at home, 26 (29%) during readmission to KCH and 23 (26%) in other health facilities. Among the 26 deaths at KCH, the leading estimated causes of death were: malaria (8, 31%), anaemia (3, 12%) and heart disease (3, 12%) (*Extended data Table S6*).

Some signs of disease severity at admission (elevated respiratory rate and presence of weak pulse), HIV infection, severe anaemia and severe wasting were positively associated with post-discharge death (*Table 3* and *Figure 2*). Malaria was negatively associated with post-discharge death (*Table 3* and *Figure 2*). Hospital admission duration was not independently associated with post-discharge death (*Extended data Table S4*).

Table 3. Multivariable regression analysis of factors associated with inpatient and post-discharge mortality.

	Inpatient analysis		Post-discharge analysis	
	Adjusted RR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Demographics				
Age in years	1.01 (1.00 to 1.02)	0.04	-	-
Clinical features at admission				
Respiratory rate per minute				
<20	2.03 (0.78 to 5.29)	0.15	_*	-
20 to 30	Reference		Reference	
>30	2.21 (1.41 to 3.47)	0.001	1.72 (1.12 to 2.63)	0.01
History of breathing difficulty	2.07 (1.40 to 3.06)	<0.001		
Weak pulse	2.18 (1.30 to 3.65)	0.003	3.54 (1.64 to 7.64)	0.001
Impaired consciousness	5.51 (3.76 to 8.10)	<0.001		
Assigned diagnosis at discharge/death				
Epilepsy/convulsions	0.30 (0.12 to 0.73)	<0.001	-	-
Investigations at admission				
HIV infected	1.75 (1.08 to 2.85)	0.02	3.06 (1.69 to 5.54)	<0.001
Malaria slide positive	-	-	0.43 (0.20 to 0.93)	0.03
Anaemia				
None	-	-	Reference	
Moderate	-	-	1.38 (0.73 to 2.61)	0.33
Severe	-	-	2.34 (1.18 to 4.63)	0.02
Bacteraemia	3.69 (2.23 to 6.10)	<0.001	-	-
Nutritional status at admission				
MUAC-for-age Z score				
≥-2	-	-	Reference	
-3 to -2	-	-	1.66 (0.95 to 2.91)	0.08
<-3	-	-	3.74 (2.24 to 6.25)	<0.001
Missing	-	-	4.99 (1.47 to 17.0)	0.01
HAZ-for-age Z score				
≥-2	Reference			
-3 to -2	0.88 (0.54 to 1.44)	0.62	-	-
<-3	2.04 (1.30 to 3.20)	0.002	-	-
Missing	1.71 (1.06 to 2.76)	0.03	-	-
Model performance				
AUC (95% CI)	0.84 (0.81 to 0.88)		0.76 (0.70 to 0.81)	
Bootstrap AUC (95% CI)	.85 (0.81 to 0.89)		0.76 (0.70 to 0.81)	

Variables are included in this table if they were selected through the backward step-wise approach and have adjusted P<0.05 for either inpatient or post-discharge analysis. All variables considered in the regression models are shown in the univariable analysis models (Table S4). MUAC, mid-upper arm circumference; HAZ, height-for-age z-score; AUC, area under receiver operating characteristics; RR, risk ratio from the log-binomial regression model; HR, hazard ratio from Cox proportion regression model, the global Schoenfeld residuals test for proportional hazard assumption P-value=0.11. *_Insufficient numbers.

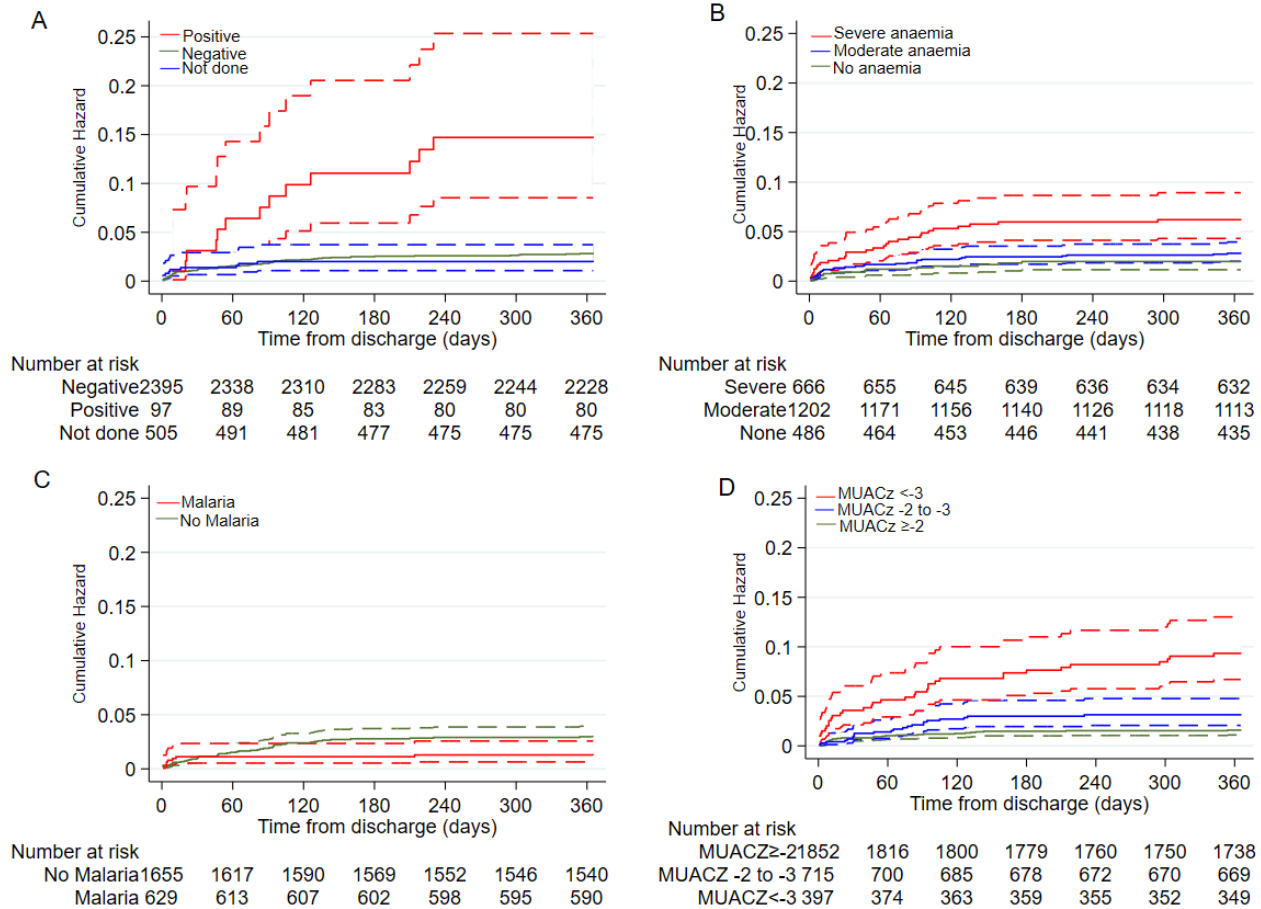


Figure 2. Cumulative hazard curves for post-discharge mortality: A) by HIV status; B) by anaemia categories; C) by malaria status and D) by mid-upper arm circumference (MUAC)-for-age z-scores groups. The broken lines are 95% confidence intervals, where there is overlap in 95%CI some lower or upper confidence intervals may not be visible.

Thirteen (0.43%) children absconded from hospital and all of them were alive after one year post-discharge.

There was no evidence that the effect of HIV infection on post-discharge mortality was modified by age ($P=0.95$), anaemia ($P=0.25$), malaria ($P=0.37$) or severe wasting ($P=0.88$). The effect of malaria on post-discharge mortality was not modified by anaemia ($P=0.33$) but was modified by severe wasting ($P=0.007$) and weak evidence of being modified by age ($P=0.05$). Compared to MUACZ ≥ -2 with a negative malaria slide, the groups of MUACZ -3 to -2 with a negative malaria slide (HR 3.60 [95%CI, 1.75 to 7.39]) and MUACz < -3 with a negative malaria slide (HR 6.36 [95%CI, 3.10 to 13.1]) had greater post-discharge mortality. Among children with positive slide results, MUACZ was not associated with post-discharge mortality.

In the exploratory analysis of biochemical variables, hyperkalaemia and elevated creatinine were associated with post-discharge mortality (*Extended data Table S7*).

Discussion

In this large study of school-aged children admitted to hospital and systematically followed-up during admission and for one year after discharge, we observed that anaemia, malaria, sickle cell disease and trauma were the leading reasons for admission. This profile is unlike that reported among under-fives, in whom pneumonia and diarrhoea are the leading reasons for admission, accounting for more than two-thirds of hospital admission in Kenya and South Africa²⁶⁻²⁸. All-cause inpatient case fatality was 3.4%, which was similar to the 3.5% previously reported in six hospitals in Kenya among children 5 to 17 years old in 2013⁵. Markers of disease severity at admission were the main predictors of inpatient mortality despite following WHO care guidelines, suggesting that current management strategies and resources may be insufficient for the sickest school-aged children. Surprisingly, epilepsy/convulsion appeared 'protective' compared to other reasons for admission in this hospitalised population, but would not be expected to be protective if compared to children in the community.

The 3.0% one-year post-discharge mortality, with almost three-quarters occurring within three months, broadly concurs with that observed in rural Mozambique three months after hospital-discharge (2.2%) among children 5 to 15 years old¹⁴, but was much lower than one-year post-discharge mortality (16%) observed among children 5 to 12 years old in Tanzania³. However, the Tanzanian study did not stratify results by age above or below 5 years and it seems likely that a higher prevalence of non-communicable diseases including cancer and heart disease reported in that population may have contributed to the higher risk of post-discharge death. However, the mortality rate of 31.2 deaths/1000 child-years observed was >34 fold higher than 0.91 deaths/1000 child-years within KHDSS among this age-group (unpublished data). The leading cause of death among the 26 children who died during readmission at KCH was malaria, similar to the leading cause assigned through verbal autopsies to children 1 to 4 years old who died in the community, but differing from that in infants among whom pneumonia was the leading causes of death in KHDSS²⁹

Tachypnoea, which may be associated with anaemia, hypoxia, sepsis or pneumonia, and weak pulse, a sign of circulatory insufficiency, were independently associated with post-discharge mortality which would suggest some children may be discharged with ongoing unstable vital signs that may lead to post-discharge deaths. Undernutrition was associated with post-discharge mortality, similar to most previous studies, which have identified nutritional status as a major risk-factor for post-discharge mortality in under-fives^{3,7,14,15,17,30}. We previously showed that MUACZ is valuable in predicting post-discharge mortality among children >5 years in a model only adjusted for age, sex and HIV status²².

We found severe anaemia was independently associated with post-discharge mortality; however, prior evidence of the effect of haemoglobin concentration on post-discharge mortality has been inconsistent, and may be influenced by the predominant causes of anaemia and local transfusion policies^{3,14,16,31–34}. Interestingly, we found no significant effect modification by anaemia on the effect of malaria on post-discharge mortality. The finding that children with malaria had lower post-discharge mortality than other reasons for admission is consistent with previous reports from this site among children <5 years of age where malaria parasitaemia had an apparently 'protective' effect on post-discharge mortality¹¹. This likely reflects the fact that when appropriately treated, mortality risk in children with malaria may be lower than in children with other causes of a similar apparent severity of illness.

In exploratory analyses, elevated creatine and hyperkalaemia, markers of impaired kidney function, were identified as predictors of both inpatient and post-discharge mortality. One study among children aged 2 to 12 years in Tanzania identified estimated glomerular filtration rate <60 ml/min/1.73m² as a predictor of one-year post-discharge mortality³. This is an important finding since dehydration and sepsis are common and associated with acute kidney injury³⁵, and current guidelines recommend potentially nephrotoxic empiric gentamicin, without

capacity for monitoring levels³⁶. However, clinical trials that could delineate attributable nephrotoxicity from background risks from renal disease, serious illness and dehydration have not yet been done.

Overall, our findings add to previous data in under-fives suggesting that hospitalisation marks an extended period of vulnerability, and reports suggesting that significant post-discharge mortality occurs outside hospital even among school-age children^{7,11,17}. The transition from inpatient to home care in the immediate three-month period following hospital discharge appears to be a critical period of risk. Risk stratification and targeted interventions for this population during this period might improve survival⁴. However, current services, such as for the management of malnutrition in the community or those to manage anaemia, largely focus on children <5 years of age and may not operate in a way that fully addresses the mortality risk in this population^{37,38}.

Strengths of this study include the large sample size, high rates of follow-up and the detailed longitudinal data available. However, this study also had some limitations. We used data from a single hospital, including only children resident within the nearby KHDSS, thus our results may not be generalizable to other sites or children living further away from the main road. Biochemical features were not systematically collected and could not be included in the primary analysis. We were not able to ascertain whether HIV infected children and malnourished children attended and complied with treatments from comprehensive care and nutrition clinics after discharge from hospital. We did not have access to causes of deaths among children who died at home or in other health facilities. Moreover, this study did not include data on caregiver or household characteristics, socio-economic situation or access to care.

Conclusion

This study highlights important differences in reasons for hospitalisation among school-aged children compared to younger children, and high rates of inpatient and post-discharge mortality among subgroups of school-aged children. To improve survival, active risk stratification and targeting intervention and follow-up in the early months after hospital discharge are needed, along with expansion of services that normally focus on the under-fives to vulnerable over-fives. The large proportion of deaths outside hospital suggests that facilitating access to healthcare among the most vulnerable, and priority clinical evaluation if unwell may be important measures.

Data availability

Underlying data

Harvard Dataverse: Replication Data for: Inpatient and post-discharge mortality among children 5-12 years old in rural Kenya. <https://doi.org/10.7910/DVN/ZJOUWB>³⁹.

The project contains the following underlying data:

- Over5years_multipleadmissions.csv (contains clinical, anthropometric, CBC, blood & CSF culture at the time of

hospital admission for children aged 5 to 12 years from 2007 to 2016, also provided in .dta format).

- over5years_khdss.csv (contains vital status in the community following hospital discharge, also provided in .dta format).
- over5yearschemistry.csv (contains the biochemistry variables that were not systematically collected at admission. This file is used to run a sub-analysis of the chemistry factors associated with both inpatient and post-discharge mortality, also provided in .dta format).
- Data_Dictionary_NgariMM.pdf (contains a list of the variables of data collected at admission and discharge and their description).
- Discharge_diagnosis_codes.csv (contain the list of codes for discharge diagnosis).

Extended data

Harvard Dataverse: Replication Data for: Inpatient and post-discharge mortality among children 5-12 years old in rural Kenya. <https://doi.org/10.7910/DVN/ZJOUWB>³⁹.

This project contains the following extended data:

- Additional_data_Mngari.et.al.2020.pdf (contains supplementary Tables S1–S5).
- Data_Readme_NgariMM.txt (dataset description and usage instructions).

- Solder_years_analysis_v1.do (STATA script used to generate the summary participants characteristics at admission, reasons for admission to hospital and inpatient mortality including factors associated with inpatient deaths).
- post-discharge_analysis_over5years.do (STATA script that runs the post-discharge analysis. It merges the Over5years_multipleadmissions.dta with the over5years_khdss.dta, computes time under follow-up, post-discharge deaths, mortality rates and factors associated with post-discharge deaths).

Reporting guidelines

Harvard Dataverse: STROBE checklist for “Replication Data for: Inpatient and post-discharge mortality among children 5-12 years old in rural Kenya”. <https://doi.org/10.7910/DVN/ZJOUWB>³⁹.

Data are available under the terms of the [Creative Commons Attribution 4.0 International](https://creativecommons.org/licenses/by/4.0/) (CC BY 4.0)

Acknowledgments

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Bruno Masquelier 

Demography Research Center, Catholic University of Louvain, Leuven, Belgium

All comments have been addressed. Thank you.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Demography.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 05 January 2021

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Matthew Wiens 

University of British Columbia, Vancouver, Canada

No new comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Post-discharge outcomes research, Epidemiology, Prediction modelling.

I confirm that I have read this submission and believe that I have an appropriate level of

expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 10 November 2020

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Matthew Wiens 

University of British Columbia, Vancouver, Canada

This is another excellent study by the Kilifi team and their colleagues which further highlights the importance of pediatric post-discharge mortality in resource limited settings, this time among a new population of children that has to date been largely neglected - school age children. I applaud this group for this new focus and believe that as evidence such as this continues to accumulate, that policy makers and others involved in the development and implementation of guidelines and recommendations, will increasingly see the provision of improved discharge and post-discharge care as a major priority to further improve child health outcomes.

This study is well justified and the reasons are well outlined in the introduction. The methodology follows a similar strategy as other previously published work by this team and is clear and concisely recorded.

Methods:

The methodology follows a similar strategy as other previously published work by this team and is clear and concisely recorded. Given that this study is retrospective in nature, and utilized data routinely collected by health workers during routine care, some mention of data quality should be considered, both in terms of standardized training, as well as quality assessment.

In terms of missing data, I see some minor statements at the bottom of Table 1, but this does not comprehensively state missingness in its totality. Would it perhaps be better to have another column in this table outlining the % missing for each for the variables of potential interest? For example, how many were missing "clinical features", how many were missing temp, how many were missing a diagnosis, etc. I recognize that some variables are defined by their presence (lethargy, decreased skin turgor, etc.), thus missingness is impossible to determine, but for those that are not subject to this issue, a report of missingness will give the readers an overall picture of the quality of the data from which these analyses are conducted. I do note that nearly 1 in 4 are missing WAZ, which does seem quite high.

For children who were below 155 months, but would be older than 155 months prior to the completion of 12 month follow-up, did these children remain in the cohort beyond the 155 month upper age limit? If yes, did the KHDSS properly capture outcomes among these older children?

Results:

The results are adequately presented given the analyses conducted. Perhaps more details could be presented on missingness in the tables.

Did the authors examine discharge disposition as an associated factor with death (i.e. discharge against medical advice).

I note that the authors mention that 45% of deaths did not occur during readmission to KCH, but does this also mean that they died outside of ANY health facility?

For those that died during a readmission, can these causes of death be briefly described?

Was any comparative exploration done on early vs late post-discharge deaths?

Was any exploration on readmissions in general done?

Discussion

The discussion touches on the main points needed for this topical area of research. I have no further comments.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Post-discharge outcomes research, Epidemiology, Prediction modelling.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 10 Dec 2020

Moses Ngari, KEMRI/Wellcome Trust Research Programme, P.O Box 230 - 80108, Kilifi, Kenya

We thank the reviewer for his comments. This has provided an opportunity to improve the manuscript. Below find point-by-point responses in italics:

This study is well justified and the reasons are well outlined in the introduction. The methodology follows a similar strategy as other previously published work by this team and is clear and concisely recorded.

Thank for the compliment.

Methods:

The methodology follows a similar strategy as other previously published work by this team and is clear and concisely recorded. Given that this study is retrospective in nature, and utilized data routinely collected by health workers during routine care, some mention of data quality should be considered, both in terms of standardized training, as well as quality assessment.

We added details about training, validation checks in the databases and measurements equipment consistency checks in the methods (study settings and Data sources/measurement)

In terms of missing data, I see some minor statements at the bottom of Table 1, but this does not comprehensively state missingness in its totality. Would it perhaps be better to have another column in this table outlining the % missing for each for the variables of potential interest? For example, how many were missing "clinical features", how many were missing temp, how many were missing a diagnosis, etc. I recognize that some variables are defined by their presence (lethargy, decreased skin turgor, etc.), thus missingness is impossible to determine, but for those that are not subject to this issue, a report of missingness will give the readers an overall picture of the quality of the data from which these analyses are conducted. I do note that nearly 1 in 4 are missing WAZ, which does seem quite high.

We already had a table of numbers missing anthropometry (Extended data Table S1). Approximately 23% of children were missing WAZ because it is in calculable for children >120 months old. WAZ has not been used in the regression analysis. We have added a new table (Extended data Table S1) with a list of variables with missing values and explained under statistical methods that anthropometric measurements and systematically collected laboratory tests were regarded as missing not at random and a 'missing' category was added in the regression models.

For children who were below 155 months, but would be older than 155 months prior to the completion of 12 month follow-up, did these children remain in the cohort beyond the 155 month upper age limit? If yes, did the KHDSS properly capture outcomes among these older children?

Yes, a child older than 155 after 12 months follow-up would still remain in study. The KHDSS census enumerates the entire population including adults. So the one-year outcome within the KHDSS was properly captured.

Results:

The results are adequately presented given the analyses conducted. Perhaps more details could be presented on missingness in the tables.

We have added an extra table with list of variables with missing values (Extended data Table s1)

Did the authors examine discharge disposition as an associated factor with death (i.e. discharge against medical advice).

We have added a sentence in the results section (under post-discharge mortality section). 13 (0.43%) children absconded from hospital and all of them were alive after one-year post-discharge.

I note that the authors mention that 45% of deaths did not occur during readmission to KCH, but does this also mean that they died outside of ANY health facility?

We have provided more details in the results section. Briefly, 40 deaths occurred at home, 26 during re-admission at KCH and 23 in other health facilities.

For those that died during a readmission, can these causes of death be briefly described?

Yes, we have provided the estimated causes of death for the 26 deaths during readmission at KCH (Extended data Table S6).

Was any comparative exploration done on early vs late post-discharge deaths?

No. We did not consider any exploration because of the few post-discharge deaths (63 Vs 26 deaths).

Was any exploration on readmissions in general done?

No. Our pre-specified endpoints were inpatient and post-discharge deaths. Hospital readmission can be examined as a separate publication.

Discussion

The discussion touches on the main points needed for this topical area of research. I have no further comments.

Thank you.

Competing Interests: No competing interests to disclose.

Reviewer Report 06 November 2020

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Duncan Hau 

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This large retrospective cohort study is of children 5-12 years of age admitted to a hospital. The authors evaluated causes of admissions and mortality of in-hospital/post-hospital up to 1 year. This study adds valuable information to the current research on post-discharge mortality, particularly for children over five years. The strengths of this study are the large participates and high follow-up rate. The authors have done a very good job presenting the data in a clear and concise form. I recommend this manuscript for indexing with a few minor revisions listed below.

Introduction:

- The authors do a thorough review of the current literature on post-hospital mortality and state the problem well.
- In Paragraph #3, the authors mention since the last review (2018), four more studies have evaluated pediatric post-discharge mortality. Reference 3 and 16 look to be from the same study subjects in Tanzania. Ref 16 evaluated the subjects based on level of hemoglobin compared to ref 3 that evaluated on diagnoses. Might want to clarify this in the text.
- Aim of study is clear. I would recommend mentioning what type of study in the last paragraph (i.e.: retrospective cohort study).

Methods:

- Methods are well written with clear study design and statistical analysis used.
- The authors mention the use of KHDSS for post-hospital period to confirm vital status post-discharge. It would be good to mention briefly how families are contacted by the KHDSS, and if children die outside the health care system (i.e.: at home), was there a way to determine cause of death?

Results:

- The results are clearly presented in text and tables/figures.
- It is interesting to note the in-patient deaths vary considerably by diagnosis (i.e.: severe pna, bacteremia, meningitis have mortality 13-17% vs. severe anaemia and malaria 4-5%). Do you know the causes of death for the post-hospital children?
- Table 3: It is interesting that epilepsy/convulsions was found to be protective for inpatient mortality. Any thoughts to elaborate this finding in the discussion?
- Post-hospital mortality 3.0% with majority of deaths (71%) within the first 3 months indicate

this is a critical period for children.

- It is interesting to note that some signs at admission you found in your study (i.e.: elevated RR, weak pulse) were associated with post-discharge death. These were also variables that were associated with in-patient death. The assumption that children are discharged from the hospital with stable vital signs (normal RR and normal pulse strength) would make me think these variables (unstable vital signs or concerning physical examination findings) would only be factors for in-patient mortality. I think in resource limited settings, some children are perhaps discharged with unstable vital signs which can lead to death post-discharge.
- The authors mentioned 45% deaths occurred without readmission to KCH. Could these children have been admitted to another health care facility in the area? I don't think we can assume they died "outside hospital" unless that was verified. This would lead back to explaining in the methods section how families were contacted post-discharge and what questions were asked.
- Do you know causes of death for the post-hospital mortality? If yes, it would be nice to know and if these differ from the admission diagnosis. For example, a child admitted for malaria was discharged and then died post-hospital due to another cause.

Discussion:

- In paragraph #6 about exploratory analyses, the authors mention ref #3 for a study that identified GFR. The authors wrote "2 to 15 years", but it appears that study evaluated 2-12 year olds. This should be corrected in the text.
- In paragraph #7 when you state "our findings add to previous data in under-fives suggesting..", shouldn't it be "over-five" since your study is on school aged children?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pediatric Hospital Outcomes Research.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 10 Dec 2020

Moses Ngari, KEMRI/Wellcome Trust Research Programme, P.O Box 230 - 80108, Kilifi, Kenya

We thank the reviewer for his comments. This has provided an opportunity to improve the manuscript. Below find point-by-point responses in italics:

Introduction:

- The authors do a thorough review of the current literature on post-hospital mortality and state the problem well.

Thank you for the compliment.

- In Paragraph #3, the authors mention since the last review (2018), four more studies have evaluated pediatric post-discharge mortality. Reference 3 and 16 look to be from the same study subjects in Tanzania. Ref 16 evaluated the subjects based on level of hemoglobin compared to ref 3 that evaluated on diagnoses. Might want to clarify this in the text

Thank you for pointing out that the two studies used the same study participants. We have highlighted this in the introduction (last sentence of paragraph 3)

- Aim of study is clear. I would recommend mentioning what type of study in the last paragraph (i.e.: retrospective cohort study).

We have added the type of study in the last paragraph of background section.

Methods:

- Methods are well written with clear study design and statistical analysis used.

Thank you for the compliment.

- The authors mention the use of KHDSS for post-hospital period to confirm vital status post-discharge. It would be good to mention briefly how families are contacted by the KHDSS, and if children die outside the health care system (i.e.: at home), was there a way to determine cause of death?

We added some description of KHDSS in the study setting section. In the results we have provided a breakdown of the location of death for the 89 post-discharge deaths. For the deaths at home or in other health facilities, we do not have access to the causes of death. We have added this as a study limitation in the last paragraph of discussion. For the 26 deaths that occurred during readmission at KCH we have added the estimated causes of deaths (Extended data Table S6).

Results:

- The results are clearly presented in text and tables/figures.

Thank you for the compliment.

- It is interesting to note the in-patient deaths vary considerably by diagnosis (i.e.: severe pneumonia, bacteremia, meningitis have mortality 13-17% vs. severe anaemia and malaria 4-5%). Do you know the causes of death for the post-hospital children?

As mentioned in previous response, we have no access to causes of deaths for deaths that occurred at home or in other health facilities. However, for the deaths that occurred at KCH, we have provided the causes in the results section.

- Table 3: It is interesting that epilepsy/convulsions was found to be protective for inpatient mortality. Any thoughts to elaborate this finding in the discussion?

Epilepsy/convulsions is only 'protective' compared to other reasons for admission. It would not be protective if comparing to the community. We have added a sentence to clarify this in the first paragraph of discussion.

- Post-hospital mortality 3.0% with majority of deaths (71%) within the first 3 months indicate this is a critical period for children.

Yes, the transition from hospital to home is a critical period for this group of children. We have this highlighted on paragraph 6 of discussion.

- It is interesting to note that some signs at admission you found in your study (i.e.: elevated RR, weak pulse) were associated with post-discharge death. These were also variables that were associated with in-patient death. The assumption that children are discharged from the hospital with stable vital signs (normal RR and normal pulse strength) would make me think these variables (unstable vital signs or concerning physical examination findings) would only be factors for in-patient mortality. I think in resource limited settings, some children are perhaps discharged with unstable vital signs which can lead to death post-discharge.

We agree, it is possible that children are discharged with unstable vital signs. However, most studies have no access to discharge clinical signs and thus not able to evaluate their effects on post-discharge outcomes. We have also highlighted this in paragraph 3 of discussion.

- The authors mentioned 45% deaths occurred without readmission to KCH. Could these children have been admitted to another health care facility in the area? I don't think we can assume they died "outside hospital" unless that was verified. This would lead back to explaining in the methods section how families were contacted post-discharge and what questions were asked.

We have responded in the previous comment. Briefly all the 40 (45%) occurred at home with another 23 (26%) occurring in other health facilities.

- Do you know causes of death for the post-hospital mortality? If yes, it would be nice to know and if these differ from the admission diagnosis. For example, a child admitted for malaria was discharged and then died post-hospital due to another cause.

We don't have access to causes of deaths for those occurring at home or in other health facilities (60, 71%) deaths. We added a table (Extended data Table S6) showing causes of deaths for the 26 deaths that occurred during readmission at KCH. Looking at the frequencies of the estimated

causes of deaths among the 26 deaths at KCH, it is likely they correlate with admission/discharge diagnosis (Malaria (8 deaths) and anaemia (3deaths) were the leading causes of deaths which were also leading causes of admission/discharge diagnosis). However, because of few numbers of causes of deaths available (29%) and possible selection bias of only including these deaths, we have not explored formal testing for diagnosis correlations.

Discussion:

- In paragraph #6 about exploratory analyses, the authors mention ref #3 for a study that identified GFR. The authors wrote “2 to 15 years”, but it appears that study evaluated 2-12 year olds. This should be corrected in the text.

Thank you for picking this, we have corrected.

- In paragraph #7 when you state “our findings add to previous data in under-fives suggesting..”, shouldn't it be “over-five” since your study is on school aged children?
As we mentioned in the background, we found no study reporting post-discharge mortality specifically on children over-five years. Therefore, the study findings extend what has been observed in under-fives. We have made the statement clearer in the discussion (paragraph 6).

Competing Interests: No competing interests to disclose.

Reviewer Report 23 October 2020

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Bruno Masquelier

Demography Research Center, Catholic University of Louvain, Leuven, Belgium

This article provides detailed and very useful information for the prevention of deaths in school-age children, showing that the experience of a hospital stay is an important marker of excess mortality in the future. I only have minor comments.

- The authors report that 3% of children died within one year period. But what is the baseline mortality rate in this age group in the Kilifi HDSS?
- The study is located within the KHDSS site. It would be nice to add some background information in the intro or discussion about the causes of death in children aged 5-12 from the verbal autopsies to compare with causes of post-discharge deaths reported in the study.
- In the methods section, it is said that details of subsequent clinic attendance were not recorded on the database. This is a bit confusing as on page 4, the authors acknowledge that children may be admitted multiple times and each child could contribute more than

one admission. Can you clarify? Are you referring to the lack of data on subsequent clinic attendance when children are admitted in other hospitals (possibly outside the HDSS) after being discharged from KCH?

- One important result is that 45% of deaths occurred without readmission to KCH. Among these, some children could have been admitted in other hospitals or in health facilities (and die before being referred to KCH). Based on info from the HDSS (e.g. verbal autopsies), is it possible to know the share of deaths that occurred outside of health facilities?
- Can you add more details about how the patient data are linked to the HDSS database? Is this record linkage deterministic based on some kind of ID number or performed on-site through searches in the HDSS database?
- The abstract states that reasons for admissions were markedly different from those reported in under-fives, but what are these? These are only mentioned very quickly in the discussion, with only two reasons (pneumonia and diarrhoea). More details should be provided on these, ideally from KCH.
- Second paragraph of the main text, "children may be admitted", please specify in the hospital or/health facilities.
- Page 3, "5 to 12" instead of '5 to12'.
- In Table 1, I don't understand why 29% of children of the sample of 3907 children were admitted prior to age 5 years as these 3907 admissions are supposed to be of children aged 5-12 years (from the description of the sample in the Results section). Can you clarify?
- In Figure 2, can you add confidence intervals around the cumulative hazard curves?

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Demography.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 10 Dec 2020

Moses Ngari, KEMRI/Wellcome Trust Research Programme, P.O Box 230 - 80108, Kilifi, Kenya

We thank the reviewer for their comments. This has provided an opportunity to improve the manuscript. Below find point-by-point responses in italics:

This article provides detailed and very useful information for the prevention of deaths in schoolmate children, showing that the experience of a hospital stay is an important marker of excess mortality in the future. I only have minor comments.

Thank you for the compliment.

The authors report that 3% of children died within one year period. But what is the baseline mortality rate in this age group in the Kilifi HDSS?

*The baseline mortality rate in this age group within KHDSS is **0.91 deaths per 1000 PYO** (Unpublished). Therefore, given our post-discharge mortality rate of 31.2 deaths per 1000 PYO, children were 34 times more likely to died compared to their community peers. We have added this in the discussion (second paragraph).*

○ The study is located within the KHDSS site. It would be nice to add some background information in the intro or discussion about the causes of death in children aged 5-12 from the verbal autopsies to compare with causes of post-discharge deaths reported in the study.

We have added some description of the causes of deaths within KHDSS assigned through verbal autopsies and a reference (<https://pubmed.ncbi.nlm.nih.gov/25377342/>) in the discussion (second paragraph).

○ In the methods section, it is said that details of subsequent clinic attendance were not recorded on the database. This is a bit confusing as on page 4, the authors acknowledge that children may be admitted multiple times and each child could contribute more than one admission. Can you clarify? Are you referring to the lack of data on subsequent clinic attendance when children are admitted in other hospitals (possibly outside the HDSS) after being discharged from KCH?

Thank for the question. We are referring to subsequent outpatient clinic attendance for management of chronic illness like HIV and TB. We have added the word "outpatient" to make the sentence clearer.

○ One important result is that 45% of deaths occurred without readmission to KCH. Among these, some children could have been admitted in other hospitals or in health facilities (and die before being referred to KCH). Based on info from the HDSS (e.g. verbal autopsies), is it possible to know the share of deaths that occurred outside of health facilities?

Yes, we have added these numbers in the results section. In brief; 40 (45%) deaths occurred at home, 26 (29%) occurred during readmission at KCH and 23 (26%) occurred in other health facilities. In the discussion we also discussed some possible causes of deaths in this age-group assigned by verbal autopsies from previous publication (<https://pubmed.ncbi.nlm.nih.gov/25377342/>).

○ Can you add more details about how the patient data are linked to the HDSS database? Is this record linkage deterministic based on some kind of ID number or performed on-site through searches in the HDSS database?

We have added more details under the study settings in the methods section.

○ The abstract states that reasons for admissions were markedly different from those reported in under-fives, but what are these? These are only mentioned very quickly in the discussion, with only two reasons (pneumonia and diarrhoea). More details should be provided on these, ideally from KCH.

We added a sentence in the methods section: study settings to the effects that ~60% of admissions at KCH are children 1 to 59 months old and majority are admitted with pneumonia and diarrhoea and provided references.

○ Second paragraph of the main text, "children may be admitted", please specify in the hospital or/health facilities.

We have added the missing words "to hospital"

○ Page 3, "5 to 12" instead of '5 to12'.

Thank you, we have corrected.

○ In Table 1, I don't understand why 29% of children of the sample of 3907 children were admitted prior to age 5 years as these 3907 admissions are supposed to be of children aged 5-12 years (from the description of the sample in the Results section). Can you clarify?

Thank for the comment, we understand this could be confusing. We have clarified in Table 1 "Had been admitted prior to age 5 years before this study"

○ In Figure 2, can you add confidence intervals around the cumulative hazard curves?

We have added 95% CI around the cumulative hazard curves as recommended (new Fig 2).

Competing Interests: No competing interests to disclose.
