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Identifying neonates at risk for post-discharge mortality in Dar es Salaam, Tanzania, and Monrovia, Liberia: Derivation and internal validation of a novel risk assessment tool

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ABSTRACT

Introduction The immediate period after hospital discharge carries a large burden of childhood mortality in sub-Saharan Africa. Our objective was to derive and internally validate a risk assessment tool to identify neonates discharged from the neonatal ward at risk for 60-day post-discharge mortality.

Methods We conducted a prospective observational cohort study of neonates discharged from Muhimbili National Hospital in Dar es Salaam, Tanzania, and John F Kennedy Medical Centre in Monrovia, Liberia. Research staff called caregivers to ascertain vital status up to 60 days after discharge. We conducted multivariable logistic regression analyses with best subset selection to identify socioeconomic, demographic, clinical, and anthropometric factors associated with post-discharge mortality. We used adjusted log coefficients to assign points to each variable and internally validated our tool with bootstrap validation with 500 repetitions.

Results There were 2344 neonates discharged and 2310 (98.5%) had post-discharge outcomes available. The median (IQR) age at discharge was 8 (4, 15) days; 1238 (53.6%) were male. In total, 71 (3.1%) died during follow-up (26.8% within 7 days of discharge). Leaving against medical advice (adjusted OR [aOR] 5.62, 95% CI 2.40 to 12.10) and diagnosis of meconium aspiration (aOR 6.98, 95% CI 1.69 to 21.70) conferred the greatest risk for post-discharge mortality. The risk assessment tool included nine variables (total possible score=63) and had an optimism corrected area under the receiver operating characteristic curve of 0.77 (95% CI 0.75 to 0.80). A score of ≥6 was most optimal (sensitivity 68.3% [95% CI 64.8% to 71.5%], specificity 72.1% [95% CI 71.5% to 72.7%]).

Conclusions A small number of factors predicted all-cause, 60-day mortality after discharge from neonatal wards in Tanzania and Liberia. After external validation, this risk assessment tool may facilitate clinical decision making for eligibility for discharge and the direction of resources to follow-up high risk neonates.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study included data on a large population of 2310 neonates discharged from hospitals in Tanzania and Liberia that allowed for generalisability of the developed risk assessment tool.
⇒ This risk assessment tool assessed 115 candidate variables, yet it is possible that there were other unmeasured confounding variables that may have influenced the variables included in the risk assessment tool.
⇒ Before clinical implementation, this risk assessment tool must be externally validated in other settings in sub-Saharan Africa.

INTRODUCTION

From 2000 to 2019, there was a dramatic reduction in mortality among children aged<5 years globally.[1] However, progress in mortality reduction has been far less pronounced for neonates aged 0–28 days.[2] Neonatal deaths make up a steadily rising proportion of child mortality, currently representing nearly half of the 5 million annual deaths among children aged <5 years.[2] The disproportionate burden of neonatal mortality has yielded a heightened focus on identifying vulnerable newborns who can be targeted for interventions to reduce neonatal mortality.[3]

Though as much as 12%–22% of neonates who are admitted to a neonatal ward in sub-Saharan Africa die during hospital admission,[4–7] the weeks to months after discharge from a neonatal ward are increasingly recognised as a vulnerable period that carries a large burden of mortality as well.[8 9] Accurately identifying neonates at risk for post-discharge

mortality is paramount in resource-limited settings as this can aid in decision-making around discharge, as well as targeted follow-up clinic visits and other interventions. However, prior risk assessment tools for childhood post-discharge mortality have largely excluded neonates, and those that have included neonates have not accounted for unique neonatal clinical factors.[10 11] Moreover, clinicians often underestimate risk of post-discharge mortality and have demonstrated a suboptimal ability to identify specific neonates at risk for post-discharge mortality using clinical judgement alone.[12 13]

Risk assessment tools provide a powerful approach to prognostication. They are derived using statistical analyses of observational data and can be used at the bedside to reduce uncertainty and improve accuracy in medical decision making.[14] Risk assessment tools can be effective across a range of settings, including those with limited resources.[15 16] To be translated into clinical practice, risk assessment tools must be rigorously derived, validated, and implemented, and their impact must be assessed in the real world. There are several validated, implemented, and generalisable risk assessment tools that are widely used in the care of children with various conditions.[17–21] However, a validated and implementable risk assessment tool to identify neonates at risk for post-discharge mortality is lacking.

Our objective was to derive and internally validate a novel risk assessment tool to identify neonates at risk for all-cause mortality within 60 days of discharge from the neonatal wards of two hospitals in sub-Saharan Africa. We hypothesised that an empirically derived set of demographic, socioeconomic, anthropometric, and clinical data from neonates could be used to identify an optimal combination of factors that would most accurately predict death in the post-discharge period.

METHODS

Study design

We conducted a prospective observational cohort study of neonates discharged from the neonatal wards at Muhimbili National Hospital (MNH) in Dar es Salaam, Tanzania and John F Kennedy Medical Centre (JFKMC) in Monrovia, Liberia. Enrolment began in October 2019 and concluded in January 2022. The protocol for this study has been published previously.[22] We adhered to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis guidelines.[23]

Patient and public involvement statement

The development of the research question was informed by the large burden of post-discharge mortality among young children in sub-Saharan Africa. Patients were not advisers in this study, nor were they involved in the design, recruitment, or conduct of the study. Results of this study will be made publicly available through open-access publication where study participants may access them.

Study setting

The neonatal mortality rate in the United Republic of Tanzania is 20/1000 live births.[24] MNH is located in the city of Dar es Salaam in the United Republic of Tanzania. MNH is supported by the Tanzanian Ministry of Health and is a national referral hospital with a catchment of >6 million people. It is also a major training site for medical students, residents, and fellows. There are approximately 5000 annual births and approximately 1100 annual admissions to the neonatal ward at MNH. Neonates who require medications, supplemental oxygen, or resuscitation are admitted to the neonatal ward. Ventilatory support via mechanical ventilation is not routinely available to neonates there.

The neonatal mortality rate is 30/1000 live births in Liberia.[24] JFKMC is located in the urban capital city of Monrovia in Liberia. JFKMC is run by the Liberian Ministry of Health, is a national referral hospital for Liberia, and has a catchment area of 1.2 million residents. It serves as the only site for paediatric education and training for medical students, residents, and fellows in Liberia. There are approximately 2500 annual births and approximately 900 annual admissions to the neonatal ward at JFKMC. Similar to MNH, neonates at JFKMC who require medications, supplemental oxygen, or resuscitation are admitted to the neonatal ward where ventilatory support is not available. Neither country has universal health insurance coverage at this time.

Study population

We consecutively enrolled neonates aged 0–28 days, regardless of their admission or discharge diagnoses, as they were discharged from the neonatal ward. Neonates aged 28 days or less at discharge were included if their caregivers (1) consented to have their hospital admission data collected, (2) had access to a phone for follow-up calls, and (3) agreed to receive follow-up phone calls. We excluded neonates who (1) died during initial hospitalisation or (2) were discharged from other wards in the hospital (eg, well-baby nursery). All participants received the standard of clinical care per the respective Ministries of Health. All clinical care was provided by the treating teams of healthcare providers and not by study staff. Study staff did not influence the clinician's independent decision to discharge a neonate in any way.

Sample size

Based on rates of post-discharge mortality reported in prior studies in specialised populations and with longer follow-up periods,[25–27] we conservatively estimated a 5% 60-day post-discharge mortality rate. However, our observed post-discharge rate was lower than estimated. Thus, using a bootstrap corrected optimism validation method, we determined that we could reasonably include 6–10 variables in a multivariable model with acceptable bias in the c-statistic, mean squared error, type 1 error, and relative bias of the estimate.[28–30]

Study procedures

In advance of the time of hospital discharge, clinicians in the neonatal wards notified our research staff of all neonates who were to be discharged. Research staff at each site approached mothers, fathers, or caregivers who were with the neonate about potential study enrolment. Prior to any data collection, caregivers provided informed written (in Dar es Salaam) or oral consent (in Monrovia). Oral consent was obtained in Monrovia because of cultural preference and low rates of caregiver literacy. Research staff interviewed caregivers of neonates to obtain demographic and socioeconomic data. Research staff also reviewed the hospital medical records to extract documented anthropometric measurements and all predetermined clinical variables.

Research staff made phone calls to caregivers of all enrolled neonates 7, 14, 30, 45, and 60 days after discharge from the neonatal ward. During these phone calls, research staff asked caregivers about each participant's vital status, any intercurrent illnesses, and any encounters with healthcare facilities after hospital discharge. In the case of post-discharge mortality, study staff arranged to visit the home to conduct a verbal autopsy with the 2016 WHO Verbal Autopsy tool.[31] Study staff who conducted verbal autopsies underwent training by WHO-trained staff prior to any data collection. All data were recorded in standardised, electronic case report forms in password-protected electronic tablets in the software SQL in Tanzania and KoboToolbox in Liberia.

Outcome

Our primary outcome was all-cause, 60-day, post-discharge mortality, identified through caregiver report during follow-up calls. Causes of death were determined by physician review of the 2016 WHO Verbal Autopsy forms and an additional physician served as an arbiter to review all forms to determine verbal autopsy determined causes of death.[31] Though prior studies have evaluated post-discharge mortality up to six or even 12 months after hospital discharge,[10 11 25] we deliberately chose 60 days as the follow-up period in this study for two reasons. First, we felt this was a reasonable timeframe to potentially link the reason for hospital admission to the post-discharge death. Second, prior studies suggest that the majority of deaths that occur post-discharge occur within the first 30–60 days after hospital discharge.[10 11 25]

Candidate variables

Prior to data collection, we identified candidate demographic, socioeconomic, anthropometric, and clinical variables thought to be potentially associated with post-discharge mortality that were consistently available at the two included sites (online supplemental table 1). We included selected variables based on the results of prior studies describing children who died after clinical encounters,[32–37] the results of modified Delphi studies in which global public health experts, paediatricians, and epidemiologists iteratively agreed on factors that could theoretically be associated with post-discharge mortality in sub-Saharan Africa,[38 39] and clinical and research experience of our research team members, who included specialists in neonatology who actively provide clinical care at each site. All variables were collected by research assistants at discharge without knowledge of the outcome.

Participant anthropometry was measured near hospital discharge using standardised digital scales for weight. Length was measured using available measuring boards and tape. All anthropometric measures were made by clinical staff who were trained in the use of the respective equipment. Neonates were classified as small (<10th percentile), appropriate (10th–90th percentile), or large (>90th percentile) for gestational age by sex according to the INTERGROWTH 21st Project standards.[40] Neonates were also categorised as low birth weight or not low birth weight according to the WHO and UNICEF recommended weight cut-off of 2500 g.[41] All vital signs (ie, heart rate, respiratory rate, etc) were taken and documented by clinical staff on the day of discharge. All variables were collected without knowledge of the potential outcome for each patient.

Statistical analyses

For the derivation of our risk assessment tool, we used all available socioeconomic, demographic, clinical, and anthropometric data collected during hospital admission to create a multivariable logistic regression model with all-cause 60-day post-discharge mortality as the outcome. We used a bivariate screen to reduce candidate predictor variables to those with p values <0.20. We then used best subset selection to identify the best-fitting model with up to 10 predictors for all-cause, 60-day post-discharge mortality. We used the model that resulted in the lowest Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC), which calculates a score accounting for how accurately the model predicts the outcome and the complexity of the model. The model with the lowest AIC and BIC indicates the model that strikes the best balance between how well the model fits the data and how complex the model is. Missing values were imputed using the chained equations algorithm in the multivariate imputation by chained equations (MICE) R package to create 10 imputed data sets.[42] Predictive mean matching, logistic regression imputation, and polytomous regression imputation were used for numerical, binary, and multicategory variables, respectively. All candidate variables were included as predictors for the MICE procedure unless a variable was represented as both numerical and categorical, in which case the numerical version was used. To account for multiple imputations and complete variable selection, we used a stacked and weighted method as described by Wood *et al*, where the 10 imputed data sets were stacked to create a single data set and individuals are weighted by one minus their fraction of missing data divided by the number of imputed datasets.[43 44]

To facilitate the use of the risk assessment tool by clinicians, we assigned weighted points to each variable by

calculating the adjusted log coefficient of each selected variable from the multivariable model, rounded it to the nearest 0.5, and then doubled the rounded log coefficients to form an integer per a widely used approach.[45–48] Variables with a negative log coefficient were assigned a score of −1. According to previously established methods, we used bootstrapping to calculate 95% CIs for likelihood ratios.[49] We used bootstrap validation with 500 repetitions to internally validate our risk assessment tool and calculate an optimism corrected area under the receiver operating characteristic curve (AUC).[50–53] In order to minimise overfitting that could occur with non-random split validation and to develop a risk assessment tool that is generalisable beyond a single site, we conducted internal validation using data from both sites.

To visualise the cumulative percentage of neonates at risk for post-discharge mortality by predicted risk we created a risk predictiveness curve. We created a calibration plot of the agreement between estimated and observed probabilities of post-discharge mortality in which an intercept of zero and a slope of one is perfect calibration.[54] In order to assess the clinical utility of our risk assessment tool, we conducted decision curve analysis comparing all included variables.[55] All analyses were performed in R V.4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) and SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

There were 2947 neonates admitted to the neonatal wards of the two hospitals during the study period; 603 (20.4%) died during their initial hospital admission. Of the remaining 2344 patients, 2310 (98.5%) were enrolled and had post-discharge outcomes available (figure 1). All participants had access to a telephone for follow-up. Neonates discharged from MNH were younger, were born to mothers with shorter gestational ages, had lower birth weights, and were more likely to be referred than those discharged from JFKMC (online supplemental table 2). Among all enrolled neonates, the median age at discharge was 8 days (IQR 4, 15 days) and 1238 (53.6%) were male (table 1). There was approximately equal enrolment at each site (49.5% [n=1145] at MNH and 50.5% [n=1165] at JFKMC).

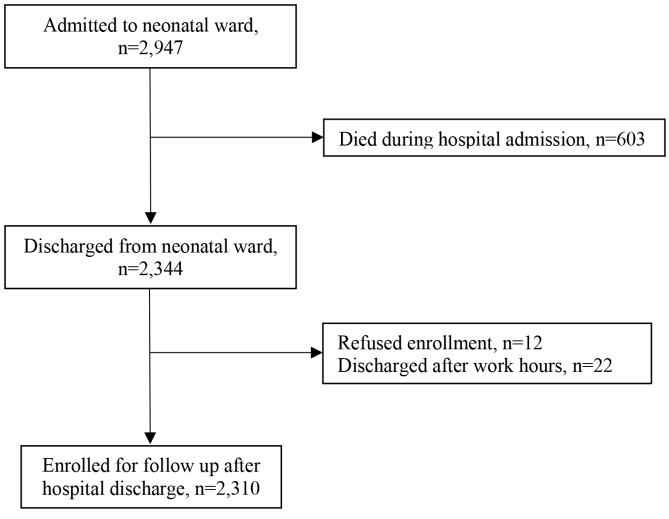

Figure 1 Flow diagram for included neonates discharged from the neonatal wards in Dar es Salaam, Tanzania, and Monrovia, Liberia.

In total, 71 (3.1%) neonates died within 60 days of discharge (n=29 in Tanzania and n=42 in Liberia). Among these, 26.8% (n=19) died within the first 7 days of hospital discharge (figure 2). Among these 19 who died within the first 7 days of discharge, the median age at discharge was 3 days (IQR 1–5.5). Of the 71 total deaths after discharge, 50.7% (n=36) occurred during a hospital readmission, 21.1% (n=15) occurred in the home, 16.9% (n=12) occurred while en route to a hospital, and 11.3% (n=8) occurred in a health centre/clinic. There was no significant difference in the time between hospital discharge and death among those who left against medical advice and those who did not (p=0.29). The most common causes of death determined by verbal autopsy review were presumed pneumonia (29.6%, n=21) and presumed congenital birth defects (22.5%, n=16) (online supplemental table 3). With the exception of carbapenams, there was no significant difference in the type of antimicrobials administered during hospital admission to neonates who died following discharge compared with those who survived (online supplemental table 4). Additionally, there was no difference in survival by type of antimicrobial prescribed at discharge (online supplemental table 5). The risk predictiveness curve demonstrated that most neonates were low risk for post-discharge mortality within 60 days of discharge (online supplemental figure 1).

Derivation of the neonatal post-discharge mortality risk assessment tool

A total of 115 variables were assessed for independent association with all-cause, 60-day post-discharge mortality (online supplemental table 1). Neonates whose caregivers took them from the hospital against medical advice (adjusted OR [aOR] 5.62, 95% CI 2.40 to 12.10), those who had meconium aspiration pneumonia (aOR 6.98, 95% CI 1.69 to 21.70), and those who had clinician diagnosed congenital birth defects (aOR 4.55, 95% CI 1.70 to 10.6) had the strongest association with post-discharge mortality (table 2). Nine variables contributed to the risk assessment tool for a total possible score that ranged from −2 to 63.

Validation of the neonatal post-discharge mortality risk assessment tool

The risk assessment tool accurately predicted post-discharge mortality among neonates (AUC of 0.77, 95% CI 0.76 to 0.80 [optimism corrected 0.77, 95% CI 0.75 to 0.80)]). A score of ≥6 demonstrated the most optimal cut point to identify neonates at risk for post-discharge mortality with a sensitivity of 68.3% (95% CI

Table 1 Characteristics of neonates discharged from referral hospitals in Dar es Salaam, Tanzania, and Monrovia, Liberia and 60-day, post-discharge outcomes

Characteristic	Overall, n=2310, n (%)	Died within 60 days of discharge, n=71, n (%)	Survived at least 60 days after discharge, n=2239, n (%)
Site			
Liberia	1165 (50)	42 (59)	1123 (50)
Tanzania	1145 (50)	29 (41)	1116 (50)
Age in days at discharge, median (IQR)	8 (4, 15)	10 (4, 18)	8 (3, 15)
(Missing)	50	5	45
Sex			
Female	1068 (46)	36 (51)	1032 (46)
Male	1238 (54)	34 (49)	1204 (54)
(Missing)	4	1	3
Prior live deliveries of mother			
0	5 (0.2)	0 (0)	5 (0.3)
1	878 (43)	25 (37)	853 (43)
2	550 (27)	12 (18)	538 (27)
≥3	626 (30)	31 (46)	595 (30)
(Missing)	251	3	248
Caregiver age (median, IQR)	27 (22, 32)	28 (23, 34)	27 (22, 32)
(Missing)	186	9	177
Family home is near hospital*	163 (8)	2 (3.4)	161 (8.1)
(Missing)	275	13	262
Pallor present during hospitalisation	75 (3.2)	7 (10)	68 (3.0)
(Missing)	1	1	0
Birth weight			
<2500 g	873 (45)	38 (58)	835 (45)
≥2500 g	1065 (55)	27 (42)	1038 (55)
(Missing)	372	6	366
Discharge body temperature			
<35.5°C	6 (0.3)	1 (1.5)	5 (0.2)
35.5°C to 37.9°C	2207 (99)	61 (94)	2146 (99)
≥38°C	23 (1.0)	3 (4.6)	20 (0.9)
(Missing)	74	6	68
Number of discharge diagnoses			
1	854 (37)	18 (25)	836 (37)
2	952 (41)	30 (42)	922 (41)
≥3	504 (22)	23 (32)	481 (21)
Congenital birth defects†	80 (3.5)	7 (9.9)	73 (3.3)
Meconium aspiration pneumonia	31 (1.3)	4 (5.6)	27 (1.2)
Haematological diseases‡	25 (1.1)	3 (4.2)	22 (1.0)
Received supplemental oxygen	497 (22)	25 (36)	472 (21)
(Missing)	39	2	37
Disposition from hospital			
Discharge	2224 (96)	60 (85)	2164 (97)
Against medical advice	85 (3.7)	11 (15)	74 (3.3)
Transfer	1 (<0.1)	0 (0)	1 (<0.1)

*Defined as living within 30 min of hospital.
†Includes congenital heart disease (eg, tetralogy of Fallot), neural tube defects, and presumed genetic disorders.
‡Includes anaemia, haemoglobinopathy, and vitamin K deficiency bleeding in a newborn.

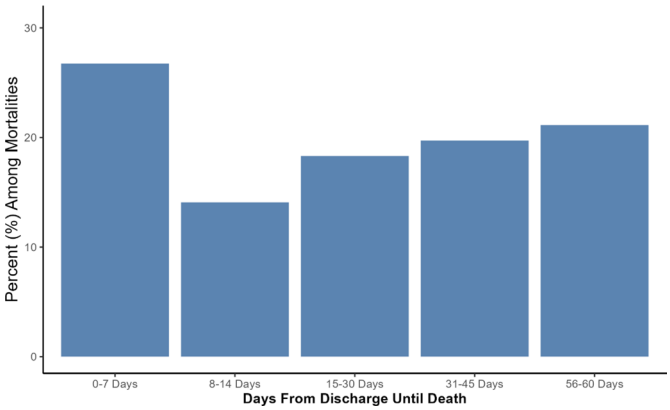

Figure 2 Percentage of neonatal deaths that occurred 0–7, 8–14, 15–30, 31–45, and 46–60 days after hospital discharge.

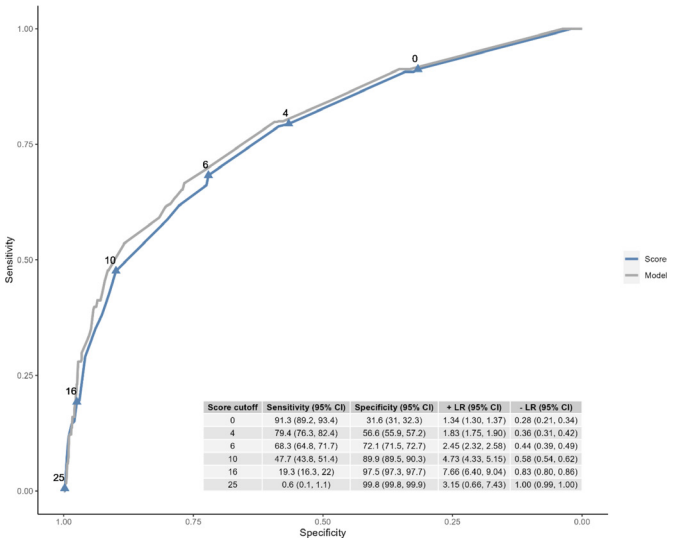

Figure 3 Receiver operating characteristic curve for risk assessment tool to identify neonates at risk for all-cause, 60-day, post-discharge mortality (n=2310). Optimism corrected area under the receiver operating characteristic curve 0.77 (95% CI 0.75 to 0.80).

64.8% to 71.5%) and specificity of 72.1% (95% CI 71.5% to 72.7%) (figure 3). A score of −2 had 100.0% sensitivity (95% CI 100.0% to 100.0%) and a score ≥25 had excellent specificity (99.8%, 95% CI 99.8% to 99.9%). Test characteristics (ie, sensitivity, specificity, positive and negative likelihood ratios, and Youden's index) for each score are included in online supplemental table 6. There was no significant difference in the time between discharge and death among those who were misclassified at the optimal risk scores (p=0.46).

Calibration and decision curve analysis

The calibration plot of our risk assessment tool for post-discharge mortality demonstrated excellent calibration for lower risk neonates but was suboptimal for high-risk neonates (online supplemental figure 2). Our risk assessment tool had a greater net benefit than each candidate variable alone in predicting post-discharge among neonates (online supplemental figure 3).

DISCUSSION

Our risk assessment tool demonstrated good discriminatory ability when internally validated and excellent calibration for low-risk neonates. The discriminatory ability of our risk assessment tool far outpaced that of clinician impression alone to identify at risk neonates.[13] Despite its enhanced discriminatory ability, the calibration was

Table 2 Components of risk assessment tool to identify neonates at risk for all-cause, 60-day post-discharge mortality in Dar es Salaam, Tanzania, and Monrovia, Liberia (n=2310)

Characteristic	Adjusted OR (95% CI)	P value	Score
Left against medical advice	5.62 (2.40 to 12.1)	<0.001	11
Mother had≥3 prior deliveries	1.83 (1.09 to 3.05)	0.021	4
Family home is near a hospital*	0.33 (0.06 to 1.04)	0.11	−1
Clinical signs			
Pallor observed by clinician	3.79 (1.32 to 9.43)	0.007	8
Low birth weight (ie, <2500 g)	3.14 (1.83 to 5.44)	<0.001	6
Discharge temperature 35.5–37.9°C	0.2 (0.08 to 0.59)	0.001	−1
Received supplemental oxygen during hospital admission	1.86 (1.07 to 3.15)	0.024	4
Diagnoses			
Meconium aspiration pneumonia	6.98 (1.69 to 21.7)	0.002	14
Congenital birth defects†	4.55 (1.70 to 10.6)	0.001	9
Haematological diseases‡	3.64 (0.72 to 13.2)	0.074	7

*Defined as living within 30 min of hospital.
†Includes congenital heart disease (eg, tetralogy of Fallot), neural tube defects, and presumed genetic disorders.
‡Includes anaemia, haemoglobinopathy, and vitamin K deficiency bleeding in a newborn.

best for low risk neonates. Although Madrid *et al* developed a model for post-discharge mortality among infants aged<90 days at discharge in Mozambique,[11] to the best of our knowledge, this is the first risk assessment tool for post-discharge mortality specific to neonates discharged from a neonatal ward. With enhanced identification of at-risk neonates, clinicians and hospitals can allocate resources to at-risk neonates to potentially avert deaths in this vulnerable time after hospital discharge.

We found that approximately one of every 32 discharged neonates died within 60 days of hospital discharge from two referral hospitals in Tanzania and Liberia and that over a fourth of those deaths occurred within 7 days of hospital discharge. The observed post-discharge mortality rate is lower than prior studies that have demonstrated rates as high as 18% among young children in sub-Saharan Africa.[9 11 25] However, there are several potential explanations for this difference. First, many prior studies that have assessed post-discharge mortality have included a longer follow-up period after hospital discharge, generally up to 6 months and even up to a year. Although a longer follow-up period may obscure the relationship between the illness that led to the index hospital admission and post-discharge mortality, it also presents more opportunity to capture post-discharge mortality. Second, prior studies on post-discharge mortality have not focused exclusively on neonates. Neonates are often followed up after hospital discharge more regularly than young children given the need for vaccinations and overall higher risk of illness,[2 56] which may have contributed to lower rates of post-discharge mortality we observed. Additionally, our study was conducted at national referral hospitals and prior studies assessing post-discharge mortality have included county hospitals in remote locations. Though not measured in our study, the quality of clinical care could have been higher in our included hospitals.

Our risk assessment tool that included practical, commonly collected clinical variables and was developed at sites in East and West Africa allows for greater generalisability than previous risk assessment tools for post-discharge mortality developed in single countries.[10 11] The optimism corrected AUC of our tool aligns with prior risk assessment tools for post-discharge mortality among young children and would be considered acceptable for clinical use and aligns with test characteristics of other risk assessment tools that have been incorporated into clinical practice.[57–61] However, because risk assessment tools perform best in their derivation set,[15] this tool must be externally validated prior to clinical use. Although there were some differences in demographics of neonates discharged from the two included sites, our risk assessment tool may be more generalisable than prior tools as this is the first to overcome the inherent limitation of single-centre studies on post-discharge mortality. Because supplemental and antimicrobial interventions targeting the post-discharge period have not demonstrated reductions in post-discharge mortality among all children,[62–65] our risk assessment tool may allow for the identification of neonatal populations in need of targeted and tailored interventions to reduce post-discharge mortality. Some factors, including living near one of these referral hospitals which was protective against post-discharge mortality, may not be modifiable. Clinicians may use such information to identify neonates at risk for post-discharge mortality.

Being diagnosed with meconium aspiration pneumonia or congenital birth defects and leaving against medical advice were most strongly associated with post-discharge mortality among neonates. Prior work in Tanzania suggests that meconium aspiration pneumonia is a major contributor to deaths among neonates.[66] Our finding of congenital birth defects conferring the risk of mortality specifically in the post-discharge period is novel, but the high burden of mortality among this population aligns with prior estimates of these defects as a leading cause of childhood mortality.[67] Deaths from congenital birth defects may increasingly confer a greater proportion of all childhood deaths as mortality from infectious causes decreases in sub-Saharan Africa.[68] Thus, neonates with congenital birth defects should be identified and prioritised for post-discharge interventions. Unlike prior studies,[10 11] known HIV infection was not associated with post-discharge mortality among neonates. This may be due to advances in maternal use of antiretroviral therapy, though future research to address this question is warranted. Discharge against medical advice is an increasingly recognised challenge. Studies suggest that it may result from inability to pay mounting hospital bills, insufficient understanding of prognosis with adequate clinical care, or perceived poor prognosis among caregivers.[69] Moreover, caregivers may have had a sense of futility of clinical care and may have decided to take their neonate home to die surrounded by family, which may have introduced potential bias into our risk assessment tool regarding leaving against medical advice.

Our results suggest that half of post-discharge deaths among neonates occurred during hospital readmission, which aligns surveillance data in Kenya.[70] We also observed that one in five post-discharge deaths within 60 days among neonates occurred in the home, which differs from other reports from Uganda that demonstrate rates of at-home post-discharge mortality as high as 45% among all children aged 0–60 months at discharge.[71] Caregivers of younger infants may be more likely to seek clinical care for neonates than for children aged 12–59 months,[72 73] which may be due to greater caregiver concern for illness among young infants compared with older children. However, as nearly one in five post-discharge deaths occurred while en route to a health facility, caregivers may not recognise symptoms early enough. Barriers to seeking healthcare for young children in sub-Saharan Africa include suboptimal access, high costs for families, and negative previous experiences with healthcare facilities.[74 75] These may be exacerbated following a costly hospital admission for a family. Further studies assessing caregiver education regarding warning

signs and symptoms that should prompt further clinical care following hospitalisation, and healthcare seeking behaviours following hospital discharge, are warranted.

Limitations

The results of our study should be considered in the context of their limitations. Our study was conducted at two national referral hospitals at two sites in Dar es Salaam, Tanzania, and Monrovia, Liberia and may not be representative of neonatal populations in other regions in sub-Saharan Africa or even in rural areas in Tanzania and Liberia. Additionally, although we included 115 candidate variables in our risk assessment tool development, it is possible that there were unmeasured variables that may have influenced the variables included in our risk assessment tool (eg, health insurance status). We could not assess the role of variable clinical care quality that neonates received. Since suboptimal clinical care quality is increasingly recognised as a contributor to childhood mortality in low-income and middle-income countries,[76] further studies are needed to assess its role in post-discharge mortality. We used observational data and thus had some missing data. However, we used robust imputation methods to overcome this limitation. Finally, as diagnostics are often limited in sub-Saharan Africa, all diagnoses were assigned by clinicians, which may not align with post-mortem causes of death determined through autopsy.[77]

CONCLUSIONS

Our risk assessment tool was a helpful predictor of all-cause, 60-day post-discharge mortality among neonates discharged from neonatal wards of referral hospitals in Tanzania and Liberia. As resource limitation may preclude the implementation of interventions for all discharged neonates, enhanced identification of high-risk neonates through our risk assessment tool may allow for more targeted interventions. After external validation, this risk assessment tool has the potential to facilitate clinical decision making focused on eligibility for discharge and the direction of resources to follow-up high risk neonates with non-modifiable risk factors.

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