

The effect of pre-existing malnutrition on pediatric burn mortality in a sub-Saharan African burn unit

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ABSTRACT

Introduction: Nutritional status predicts burn outcomes in the developed world, but its effect on burn mortality in the developing world has not been widely studied. In sub-Saharan Africa, burn is primarily a disease of children, and the majority of children in sub-Saharan Africa are malnourished. We therefore sought to determine the prevalence and effect of malnutrition on burn mortality at our institution.

Methods: This is a retrospective review of children aged 0-5, with anthropomorphic measurements available, who were admitted to our burn unit from July 2011 to May 2016. Age-adjusted Z scores were calculated for height, weight, weight for height, and mid-upper arm circumference (MUAC). Following bivariate analysis, we used logistic regression to construct a fully adjusted model of predictors of mortality.

Results: Of the 1357 admitted patients, 839 (61.2%) were aged 0-5. Of those, 512 (62.9%) had one or more anthropomorphic measurements available, and were included in the analysis. 54% were male, and the median age was 28 months. The median TBSA was 15%, with a majority of burns caused by scalds (77%). Mortality was 16%. Average Z-score for any of the indicators of malnutrition was -1.45 ± 1.66 . TBSA (OR: 1.08, 95% CI: 1.06, 1.11), decreasing Z-score (OR: 1.19, 95% CI: 1.00, 1.41), and flame burn (OR: 2.51, 95% CI: 1.40, 4.49) were associated with an increase in mortality.

Conclusion: Preexisting malnutrition in burn patients in sub-Saharan Africa increases odds of mortality after controlling for significant covariates. Survival of burn patients in this region will not reach that of the developed world until a strategy of aggressive nutritional support is implemented in this population.

1. Introduction

Burn disproportionately affects the developing world, with over 90% of global burn mortality occurring in low- and

middle-income countries (LMICs). In sub-Saharan Africa (SSA), burn is predominantly a pediatric disease, with 60% of overall mortality affecting the 0-15 age group [1]. The sub-Saharan Africa region is responsible for 64 and 78% of the

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world's burn deaths in children aged 0-4 and 5-14, respectively [2-5].

The hypermetabolic effect of burns is well documented [6-9]. Patients with severe burns can lose up to 25% of their lean body mass after an acute burn [8,10], and losses of lean body mass can occur despite nutritional intervention. Children are especially vulnerable, given their smaller reserve and increased caloric and protein requirements in relation to body size [11,12]. Optimization of nutritional status following burn is an essential intervention in high income country (HIC) burn units, where the prevalence of malnutrition in the general population is low. Interestingly, in LMICs, where baseline prevalence of malnutrition is much higher, there is a paucity of data regarding the effect of pre-existing malnutrition on burn mortality [13].

The World Health Organization (WHO) defines moderate pediatric malnutrition as a weight-for-age between -2 and -3 Z-scores below the median of the WHO growth standards; moderate wasting and stunting are described as weight-for-height and height-for-age falling between -2 and -3 Z-scores, respectively [14]. The Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN) have also established a set of indicators for the diagnosis of under-nutrition in patients aged 1 month to 18 years. For patients with only one anthropomorphic measurement available, mild and moderate malnutrition are defined by Z-scores falling between -1 and -1.9 ; and -2 and -2.9 , respectively, for weight-for-height-for-age; body-mass-index-for-age; or mid-upper-arm-circumference (MUAC)-for-age. For patients who are followed over time, additional indicators include decline in weight gain velocity (<2 years of age), weight loss (2-20 years of age), deceleration in weight-for-height Z-score, and inadequate nutrient intake [15,16].

The prevalence of malnutrition in children living in SSA is high [12,14,17]. Malawi, a landlocked country in southeastern Africa, is one of the poorest nations in the region, with a 2015 per capita gross domestic product (GDP) of \$350. Its human development index (HDI) puts it 173rd out of 186 countries in the world. Life expectancy is 62 years at birth [18]. As of 2015, 20.7% of the population could not meet the minimum daily energy consumption, and in 2010, 72.2% of the population lived below \$1.25/day. The prevalence of underweight (weight for age Z-score <-2) in children 0-5 living in Malawi worsened between 2009 and 2014, from 12.1 to 16.7% [17].

Because of the confluence of the high malnutrition prevalence and burn mortality in LMICs, we hypothesize that the presence of pre-existing malnutrition in children age ≤ 5 years presenting with burn is associated with increased mortality in a sub-Saharan Africa burn unit.

2. Methods

We performed a retrospective review of prospectively collected data entered into the Kamuzu Central Hospital (KCH) burn unit database. KCH, located in Malawi's capital of Lilongwe, is a public, 600-bed, tertiary care hospital with a catchment population of approximately 5 million people. The KCH burn

unit was commissioned in 2011 in partnership with the North Carolina Jaycee Burn Center. It has 31 beds, 8 nurses, 2 nursing assistants, and 1-2 clinical officers, who oversee clinical management and perform surgeries with attending surgeon oversight [5].

Children aged 0-5 years old who were admitted to the burn unit between 1 July 2011 and 1 May 2016 were included in this study. The primary aim was to determine the relationship between pre-existing malnutrition, defined using the WHO and AND/ASPEN indicators, and burn mortality. Primary outcome was mortality among pediatric patients admitted to the burn unit during the period under study.

We examined demographic and clinical characteristics of the entire cohort, as well as between patients with and without anthropomorphic measurements. Only children with anthropomorphic measurements were then included in the bivariate analysis of variables that correlated with mortality. Bivariate analysis was performed on each of the independent variables based on mortality outcome, using Pearson's correlation, two tailed Fisher's exact test, 2-sample t-test, or Kruskal-Wallis testing, as appropriate. Means are presented with standard deviations and medians with interquartile ranges (IQR). All of the variables found to significantly affect mortality in bivariate analysis, as well as variables with a significantly unequal distribution among the measured and unmeasured groups, were used in multivariate logistic regression to construct a fully adjusted model of significant predictors of mortality. This multivariate logistic regression model was applied only to children with anthropomorphic measurements.

Currently, dates of birth are not routinely collected. Instead, parents report patient ages in months for approximately the first 18 months, and years thereafter. We therefore assigned a conservative age estimate (equal to the year plus 0 months) and a liberal one (equal to the year plus 6 months) for all children aged 1-5 who did not have exact ages in months reported on admission, and performed two Z-score calculations for all of the indicators. Total body surface area burned (% TBSA) is currently assessed twice: once in the casualty department, and the second upon arrival on the burn ward. Because there was no statistically significant difference between these measurements, TBSA measured in the casualty department was used for this analysis. The 46 absconders (5.5% of patients, evenly distributed among the two groups) were included in the "living" category for the purposes of the final outcome.

All statistical analysis was performed using STATA/SE 13.1 (StataCorp LP, College Station, TX). Age-adjusted Z-scores were calculated for height, weight, and weight-for-height, using the STATA zscore06 package [20], which is based on 2006 WHO data. MUAC-for-age Z score was calculated using WHO software available online, based on 2007 WHO data [21]. Z-scores lower than -6 standard deviations (SDs) of the mean for height, weight, and lower than -5 SDs for weight for height for age and MUAC for age, were dropped from subsequent analysis, per WHO recommendations [22]. After removing outlying Z-scores, we constructed a combined Z-score variable using the available indicators of malnutrition as recommended by WHO, AND, and ASPEN. Because there was no statistical difference in Z-scores or age distribution based on

the conservative versus liberal age estimates, only one set is reported here for ease of interpretation.

3. Results

1357 patients were admitted to the burn unit at KCH between 1 July 2011 and 1 May 2016. Of these, 839 (61.2%) were aged 0-5. Median age of this group was 28 months, and 54% were male. Median TBSA was 15% (9%-23%) and the prevailing mechanism of injury was scalds (77%). 512 (62.9%) of the children had one or more anthropomorphic measurements available. 428 patients (83.6%) had the measurements performed within 3 days of admission (IQR: 2-5 days). Time to first measurement was not significantly correlated with the primary outcome ($p=0.470$), and did not affect Z-score ($p=0.203$). Mean Z-score for any of the indicators of malnutrition was -1.45 ± 1.66 . 63% of all children met the criteria for mild malnutrition (66% males and 59% females), and 38% for moderate malnutrition (42% males and 34% females).

We compared patients with and without anthropomorphic measurements with respect to demographics, mechanism of burn, year of admission, and outcome (Table 1). The measurement group had significantly more males (57% versus 50%, $p=0.049$); higher median TBSA (15% versus 12.25%, $p=0.004$); was admitted more often in the later years of the study ($p<0.001$); and had a longer median length of stay

(14 days versus 8, $p=0.001$). The two groups did not differ with respect to age, mechanism of burn, comorbidities, HIV status, the administration of antibiotics on admission, the use of traditional medicine, time to presentation, operative or conservative management, or the final outcome.

Bivariate analysis of variables associated with mortality was performed using patients with anthropomorphic measurements available (Table 2). 80 (16%) of the patients died. Mortality did not differ with year of admission. On average, patients who lived had a mean TBSA of $14.6 \pm 10\%$, whereas those who died had a mean TBSA of $30.5 \pm 18\%$ ($p<0.001$); survivors also had a longer length of stay (20 ± 23 days versus 12 ± 12 days, $p<0.005$). The median time to death from admission was 9 days [2-19]. Independent variables associated with mortality were: %TBSA, mechanism of burn, and Z-score. Flame burns and scald burns resulted in 27% and 13.6% mortality, respectively ($p<0.001$). There were no statistically significant differences in mortality based on age, comorbidities, HIV status, antibiotics administration, traditional medicine use, time to presentation, or rate of surgical intervention.

Multivariate logistic regression was performed only in children with anthropomorphic measurements available. After adjusting for significant covariates in the final model, increasing TBSA (OR: 1.08, 95% CI: 1.06, 1.11), flame burn (OR: 2.51, 95% CI: 1.40, 4.49) and decreasing Z-score by 1 (OR: 1.19, 95% CI: 1.00, 1.41) were associated with increased

Table 1 – Characteristics of patients aged 0-5 at KCH burn unit.

Variable	Entire cohort N=839	Measurement group ^a N=512	No measurement group N=327	p value
Baseline characteristics				
Gender				0.049
Male	454 (54.2%)	291 (57%)	163 (50%)	
Female	383 (45.8%)	220 (43%)	163 (50%)	
Age, conservative				0.857
Median (range)	26 (18, 36)	26 (18, 36)	26 (18, 36)	
Age, liberal				0.951
Median (range)	30 (18, 42)	30 (18, 42)	30 (18, 42)	
Comorbidities				0.374
None	759 (93.5%)	461 (92.4%)	298 (95.2%)	
Epilepsy	27 (3.33%)	18 (3.6%)	9 (2.88%)	
Pre-existing malnutrition	18 (2.22%)	14 (2.81%)	4 (1.28%)	
Other	8 (1%)	6 (1.2%)	2 (0.64%)	
HIV status				0.718
Nonreactive	137 (17%)	80 (16.4%)	57 (17.9%)	
Reactive	4 (0.5%)	3 (0.6%)	1 (0.3%)	
Unknown	666 (82.5%)	406 (83%)	260 (81.8%)	
Admission year				<0.001
2011	96 (11.4%)	44 (8.59%)	52 (15.9%)	
2012	169 (20.1%)	41 (8%)	128 (39%)	
2013	164 (19.6%)	117 (22.85%)	47 (14.4%)	
2014	181 (21.6%)	147 (28.7%)	34 (10.4%)	
2015	160 (19.1%)	116 (22.7%)	44 (13.5%)	
2016	69 (8.2%)	47 (9.18%)	22 (6.7%)	
Burn characteristics				
%TBSA				0.004
Median (range)	15% (9, 23)	15% (9, 25)	12.25% (7.4, 20)	
Time to presentation				

Table 1 (continued)

Variable	Entire cohort N=839	Measurement group ^a N=512	No measurement group N=327	p value
<24h	568 (70%)	348 (69.6%)	220 (70.7%)	0.549
24-48h	34 (4%)	24 (4.8%)	10 (3.2%)	
>48h	209 (25.8%)	128 (25.6%)	81 (26.1%)	
Days to presentation ^b				0.976
Median (range)	6 (4, 12)	6 (3, 14)	6 (4, 10)	
Mechanism				0.464
Scald, water	477 (57.2%)	294 (57.5%)	183 (56.7%)	
Scald, other	165 (19.8%)	96 (18.8%)	69 (21.4%)	
Flame	186 (22.3%)	119 (23.3%)	67 (20.7%)	
Contact	4 (0.5%)	1 (0.2%)	3 (0.9%)	
Electrical	2 (0.2%)	1 (0.2%)	1 (0.3%)	
Cause				0.050
Playing	25 (3%)	15 (3%)	10 (3.1%)	
Clothes caught fire	97 (11.7%)	58 (11.4%)	39 (12.1%)	
Cooking with/fell into hot liquid	521 (62.8%)	304 (60%)	217 (67.1%)	
Cooking with/fell into fire	76 (9.16%)	48 (9.5%)	28 (8.7%)	
Other	111 (13.4%)	82 (16.1%)	29 (9%)	
Intervention				
Traditional medicine				0.737
Yes	123 (16%)	71 (14.8%)	52 (18%)	
No	647 (84%)	408 (85.2%)	239 (82%)	
Antibiotics on admission				0.976
Yes	569 (69.5%)	348 (69%)	221 (70%)	
No	250 (30.5%)	156 (31%)	94 (30%)	
Surgery				0.640
Yes	186 (22.2%)	123 (24%)	63 (19.3%)	
No	653 (77.8%)	389 (76%)	264 (80.7%)	
Outcomes				
Length of hospital stay				
Median (range)	11 (7, 24)	14 (8, 28)	8 (3, 14)	<0.001
Disposition				0.712
Lived	689 (83.6%)	420 (84%)	269 (83%)	
Died	135 (16.4%)	80 (16%)	55 (17%)	

^a Patients with any anthropomorphic measurements available (weight, height and/or MUAC).

^b If delayed >48h.

odds of mortality (Table 3). For every decrease in Z score by 1 standard deviation, the odds of mortality increased by 20%. Fig. 1 depicts the adjusted model.

4. Discussion

It is well recognized that the metabolic demands and energy requirements during burns are satisfied at the expense of lean body mass (LBM) [23], and that muscle protein catabolism exceeds synthesis among patients with burns [24]. We show in this study that in the presence of pre-existing malnutrition and burn, odds of mortality increase. This, we believe, is attributable to the burn acceleration of severe protein energy malnutrition, which further compromises wound healing.

Because many burn victims do not seek medical attention in SSA, the true incidence of burn in the region is unknown [3,4]. However, in South Africa alone, 3.2% of the population is

estimated to suffer burns annually [13]. Most studies show a predominance of the very young (under 5 years) in the SSA burn patient population [3-5,25]. Whereas in the developed world a pediatric burn patient is expected to survive burns in excess of 90% TBSA, in the absence of inhalation injury and with appropriate hospital support [8,9], burn outcomes in SSA continue to lag behind the developed world. Although the majority of admissions have a TBSA <30%, the overall mortality ranges from 10% to 26.8% [4]. Many reasons have been cited for this lag, including the lack of dedicated burn units, complexity and expense of specialized burn care, and the general scarcity of medical providers in the region [3,4,13,26]. Factors consistently associated with mortality in SSA burn patients are TBSA burned, age, mechanism of injury, and inhalation injury [3-5,26-31]. Our study shows that baseline nutritional status of pediatric burn patients also contributes to mortality, representing an easily modifiable factor among those risks.

Table 2 – Bivariate analysis of mortality risk factors.

Variable	Lived N=419 (82%)	Died N=80 (16%) ^a	p value
Demographics			
Gender			
Male	244 (58.2%)	39 (48.8%)	0.117
Female	175 (41.8%)	41 (51.3%)	
Age, in months			
Mean (\pm St Dev)	31.6 (16.3)	33.1 (15.4)	0.440
Comorbidities			
None	382 (92.9%)	69 (90.8%)	0.511
Epilepsy	15 (3.65%)	3 (3.95%)	
Malnutrition	11 (2.68%)	2 (2.63%)	
Other	3 (0.73%)	2 (2.63%)	
HIV status			
Nonreactive	69 (17.1%)	10 (13.2%)	0.040 ^b
Reactive	1 (0.25%)	2 (2.63%)	
Unknown	334 (82.7%)	64 (84.2%)	
Admission year			
2011	36 (8.59%)	8 (10%)	0.676
2012	33 (7.88%)	8 (10%)	
2013	97 (23.2%)	16 (20%)	
2014	117 (27.9%)	27 (33.8%)	
2015	97 (23.2%)	17 (21.3%)	
2016	39 (9.31%)	4 (5%)	
Burn characteristics			
%TBSA			
Median (range)	14% (9, 20)	28% (19, 36)	<0.001
Timing from injury to presentation			
<24 h	287 (70%)	55 (71.4%)	0.897
24-48 h	21 (5.12%)	3 (3.90%)	
>48 h	102 (24.9%)	19 (24.7%)	
Days to presentation			
Median (range) ^c	5 (3, 11)	7 (4, 17)	0.883
Mechanism			
Scald	333 (79.7%)	47 (58.8%)	<0.001
Flame	85 (20.3%)	33 (41.3%)	
Intervention			
Traditional medicine use			
Yes	56 (14.1%)	12 (17.4%)	0.476
No	341 (85.9%)	57 (82.6%)	
Antibiotics on admission			
Yes	283 (68.5%)	57 (73.1%)	0.424
No	130 (31.5%)	21 (26.9%)	
Surgery			
Yes	100 (23.9%)	21 (26.3%)	0.649
No	319 (76.1%)	59 (73.8%)	
Nutritional indicators			
Height-for-age Z-score			
Median (range)	N=198 -2.22 (-3.31, -0.75)	N=40 -2.86 (-3.62, -1.49)	0.067
Weight-for-age Z-score			
Mean (\pm St Dev)	N=385 -0.63 (1.45)	N=64 -0.83 (1.40)	0.301
Weight-for-height z-score			
Mean (\pm St Dev)	N=180 0.68 (1.62)	N=27 0.95 (1.26)	0.404
MUAC-for-age Z-score			
Median (range)	N=275 -0.16 (-0.93, 0.61)	N=40 -0.57 (-0.96, 0.61)	0.467
Combined Z-scores			
Median (range)	N=415 -1.51 (-2.67, -0.41)	N=78 -1.68 (-3.35, -0.5)	0.048

^a 12 patients did not have an outcome recorded.

^b Omitted from final model because of the extremely small number of patients.

^c If delayed >48h.

Table 3 – Odds ratios for the fully adjusted logistic regression model.

Variable	Odds ratio (95% confidence interval)
Flame burn	2.70 (1.51, 4.83)
Poor nutritional status	1.19 (1.0, 1.42)
TBSA	1.08 (1.05, 1.11)
Age ^a	1.14 (0.36, 4.94)
Year of admission ^a	0.92 (0.75, 1.13)

^a Included because of uneven distribution among the measurement and no measurement groups.

Pediatric malnutrition in SSA is a well-known entity. Most of the research and intervention in the region has been focused on the edematous and non-edematous forms of severe malnutrition (marasmus and kwashiorkor, respectively), in spite of the fact that mild and moderate malnutrition significantly increases the risk of mortality in children [14,32]. The WHO estimates that 56% of deaths in children 6-59 months are attributable to malnutrition, and the majority of those (83%) to its mild or moderate, and not severe, form [12]. Mildly, moderately, and severely underweight children are 2.5, 4.6, and 8.4 times as likely to die from infectious diseases as normal weight children [32].

There is a paucity of data examining malnutrition and its effect in pediatric burn or surgical patients in SSA. Two studies have examined nutrition in sub-Saharan Africa burn units [11,13], both from South Africa. A study of 67 South African patients from a rural area of the Eastern Cape reported baseline malnutrition in 46.3% of children under 8, defined using the WHO indicators, and found that nutritional status worsened during hospital stay, but did not find an association of malnutrition with mortality [13]. Vijfhuize et al. examined the feeding practices and nutritional intake in a dedicated pediatric burn unit at the Red Cross War Memorial Children's

Hospital in Cape Town, and found that even with a dedicated nutritionist, supplements, and enteral feeding available, 9 out of 11 patients with burns >20% of TBSA, and 19 out of 29 patients with smaller burns, did not have sufficient daily caloric intake [11]. This study was not aimed at reporting nutritional indicators or patient outcomes.

Our study is limited by its retrospective methodology. In the absence of adequate burn analgesia, height measurement can be challenging for children with extremity or truncal burns, who are unable to extend fully due to pain. This may have resulted in a shorter measured height relative to the true height, potentially affecting the child's Z-score for height-for-age and weight-for-height. Using one data point for anthropomorphic measurements can introduce an element of imprecision, as patients may be weighed wearing their clothing and with bulky dressings, inappropriately adding to their weights and increasing their Z-scores. This is particularly true for larger burns, which utilise more dressings. Thus it is possible that the true level of malnutrition in our burn unit is underestimated. Another important limitation is the absence of laboratory findings and vital signs to exclude burn sepsis. This reflects the resource constraints and technical limitations inherent in this extremely resource-poor setting. However, our study is strengthened by the fact that all patients are cared for in a dedicated burn unit, minimizing any confounding due to the standard of care. The study population is large, and data collection methods standardized across the study period. Furthermore, the majority of patients had anthropomorphic measurements performed at admission or soon thereafter, minimizing the influence of infectious processes or in-hospital malnutrition on the outcome. Although not all patients had every anthropomorphic measurement available, by combining any of the recommended WHO/AND/ASPEN indicators, we were able to construct a nearly complete nutrition variable.

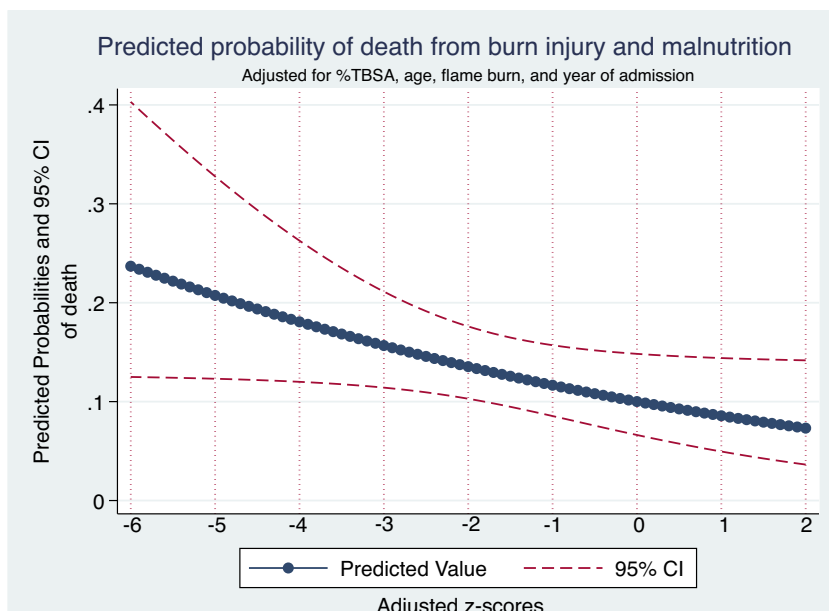


Fig. 1 – Predicted probability of death in patients with malnutrition adjusted from %TBSA, age, flame burn and year of admission.

5. Conclusion

We have demonstrated that preexisting malnutrition is an independent and modifiable risk factor for burn mortality in children in a resource-poor setting. Even with enhanced medical and surgical care, burn outcomes in LMICs will continue to lag behind HICs if the baseline malnutrition is not addressed with an aggressive nutrition enhancement strategy immediately following burn. The allocation of resources to provide optimal nutritional support is imperative in burn units in LMICs, where malnutrition prevalence is high. Nutritional intervention represents an essential strategy to improve burn survival in resource-poor settings, particularly in children.

Conflict of interest

The authors declare that they have no conflict of interest.

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