Short-term Prognosis in Severe Adult and Adolescent Malnutrition During Famine

Use of a Simple Prognostic Model Based on Counting Clinical Signs

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Context In the setting of famine, infection is likely to cause mortality among severely malnourished persons. Although clinical signs are likely to be useful prognostic indicators in this setting, use of a clinical assessment model has not been studied.

Objective To examine the use of clinical signs in the prediction of short-term mortality in severely malnourished adults and adolescents during famine.

Design Retrospective cohort study.

Setting Concern Worldwide Adult Therapeutic Feeding Center in Baidoa, Somalia.

Patients Data from the clinical records of 383 adult and adolescent inpatients admitted to the center between November 1992 through March 1993 who were aged 15 years or older and had a body mass index (BMI) of 13.5 kg/m^2 or less or any signs of edematous malnutrition.

Main Outcome Measures Association of mortality with presence or absence of 8 clinical signs (edema, hydration, ascites, dysentery, diarrhea, anemia, chest infection, and ability to stand) and BMI at admission, and sensitivity and specificity of models including a count of clinical signs and BMI in the prediction of mortality at the center.

Results Ninety-one patients (23.8%) died, with a median time to death of 8 days from admission. Of the 8 clinical signs, severe edema (unadjusted odds ratio [OR], 2.45; 95% confidence interval [CI], 1.41-4.27), apparent dehydration (unadjusted OR, 2.73; 95% CI, 1.60-4.66), and inability to stand (unadjusted OR, 2.96; 95% CI, 1.40-6.26) were independently associated with mortality. The most useful clinical model was that based on the presence of any 1 of these 3 signs, with a sensitivity of 77% and a specificity of 59%. Ability of admission BMI to predict mortality was less than random.

Conclusions Models based on clinical signs predicted death better than BMI. Simple counts of clinical signs performed as well as more complex models based on the addition of ORs. Counting relevant clinical signs is an easy and effective prognostic tool in severe adult and adolescent malnutrition during famine; however, it is not sensitive enough for use as a screening tool.

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FOR MANY YEARS, IT HAS BEEN RECognized that malnutrition increases both susceptibility to and severity of infection. Vitamin, mineral, and other dietary deficiencies, depressed cell-mediated and humeral immunity, gastric acidity, mucosal integrity, and altered flora are all known to increase susceptibility to infection.[1,2] The situation in famine is usually worsened by a breakdown in public health infrastructure and congregation of displaced people in crowded and unhygienic conditions.[3] In situations of malnutrition in developed countries, exhaustion of fat or fat-free mass is most often the terminal event,[4,5] but the combination of poor public health environment and immunosuppression in famine means that it is infection, rather than absolute loss of fat or fat-free mass, that kills people.

The strong association between infection and mortality indicates that clinical signs are likely to be useful prognostic indicators. Clinical models for prediction of mortality, useful in the screening of admission to child feeding centers, have been proposed.[6] Although reported to be effective in identifying children at high risk of mortality,[7] these models have been criticized because interactions between the features used, such as edema and hypoproteinemia, were not taken into account.[8] In adults, the use of clinical models to assess nutritional status appears to have been restricted to well-nourished surgical patients.[9] To date, similar assessments have not been made in severely malnourished adults or during famines.

Extreme conditions often characterize famine relief programs. Levels of need are high and trained staff, equipment, and buildings are scarce. Some-

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Table 1. Characteristics of the Study Population*

Variables	All Patients (N = 383)	Survivors (n = 292)	Nonsurvivors (n = 91)
Self-reported age, mean (SD) [range], y	33.0 (16.0) [15.0-89.0]	32.7 (14.8) [15.0-89.0]	33.8 (16.5) [15.0-80.0]
Sex			
No.	382	292	90
Male, No. (%)	185 (48.4)	140 (47.9)	45 (50.0)
Female, No. (%)	197 (51.6)	152 (52.1)	45 (50.0)
BMI, kg/m^2			
No.	296	244	52
Mean (SD) [range]	12.7 (2.0) [9.0-24.0]	12.6 (2.0) [9.0-24.0]	12.9 (1.9) [9.3-17.6]
Weight, kg			
No.	341	271	70
Mean (SD) [range]	34.0 (7.2) [19.2-59.5]	34.0 (7.2) [21.0-59.5]	34.1 (7.4) [19.2-53.4]

*No. for sex, BMI (body mass index), and weight indicates how many persons for whom data were available.

times, crowds of several thousand people may gather, attempting to gain admission to centers. Such centers may become overfilled, disorganized, and dysfunctional if patient selection and prioritization is not efficient. Tools to assess patients must be quick, simple, and reliable, even when used by minimally trained staff, who may be barely literate. This study investigates the effectiveness of 2 assessment tools, body mass index (BMI) and models using readily ascertainable clinical signs, during the height of a major famine.

METHODS

Subjects

This retrospective cohort study involved clinical record data of 393 patients admitted to the Concern Worldwide Adult Therapeutic Center, Baidoa, Somalia, between November 4, 1992, and March 15, 1993. Criteria for inclusion in this retrospective analysis were a BMI at admission of 13.5 kg/m^2 or less or any signs of edematous malnutrition, a reported age of 15 years or older, the presence of an inpatient treatment and clinical data card, and no record that the patient was admitted because of medical criteria alone. Of these 393 patients, 10 were excluded owing to the absence of outcome data. The mean reported age of the remaining 383 subjects was 33.0 years, with no significant age difference between sexes (t_{380}=1.32; P=.19). Of those admitted, 48.4% were men (TABLE 1). Mean (SD) BMI at admission was 12.7 (2.0) kg/m^2; mean (SD) weight was 34 (7.2) kg. Mean admission BMI of survivors was 12.6 kg/m^2 vs 12.9 kg/m^2 for nonsurvivors.

Center, Staff, and Equipment

The therapeutic feeding center consisted of 9 stick shelters with plastic sheeting roofs and mud floors. Separate shelters were designated for new admissions, those with edematous malnutrition, those with dysentery, and those suspected of having pulmonary tuberculosis. Beds were not available and all patients had to lie on plastic sheets on compacted mud floors.

The center was staffed by 1 expatriate physician, 1 to 2 expatriate nurses, 3 local nurses, and approximately 30 other helpers and cooks. High levels of supervision were maintained, with staff-patient ratios of 1:8 or less, particularly during the first few days after admission. These staff members distributed food and oral rehydration solution (ORS), encouraged patients to eat and drink, and helped feed those who were unable to feed themselves.

A set of standard Hanson spring scales and a locally constructed height board were used to weigh and measure patients. The scales were calibrated in London, England, and Baidoa using known weights. Results were similar at both sites. In the useful range of 20 to 50 kg, there was a linear increase in error (r=0.99). A correction factor derived using ordinary least squares linear regression was used to correct each weight measurement.

Medical Treatment

Oral antibiotics were needed by the majority of patients on admission, with many patients continuing to receive an antibiotic throughout their stay in the center. Penicillin V and ampicillin were the first-line antibiotics for pulmonary infection, as were trimethoprim-sulfamethoxazole and metronidazole for dysentery and persistent diarrhea. Chloramphenicol was the only second-line antibiotic used.

Discharge criteria were predominantly clinical. Freedom from infectious disease, a good appetite, constant weight gain, and ability to walk and care for oneself were all necessary conditions for discharge. The presence of minimal pedal edema did not preclude discharge as long as these criteria were met. On discharge, transport to patients' home villages was provided.

Dietary Treatment

Patients were orally rehydrated using the World Health Organization formula for ORS (sodium chloride, 3.5 g/L; trisodium citrate, 2.9 g/L; potassium chloride, 1.5 g/L; and glucose, 20 g/L). All patients were given 6 to 8 meals per day. Diets consisted of high-energy milk (made from dried skimmed milk, vegetable oil, and sugar), sweet tea, rice, oil, beans, biscuits, and local fruits, especially bananas. During the first few days after admission, the high-energy milk component was diluted with ORS to reduce the incidence and severity of watery diarrhea and vomiting that is often associated with the early stages of refeeding severely malnourished persons. The degree to which the high-energy milk was diluted was tailored according to severity of diarrhea.

Two therapeutic diets were used in the center. For the higher-protein diet, patients were offered 156 g of protein and 16.5×10^3 kJ (16% of energy from protein; protein-energy ratio, 9.5 mg/kJ per day) each day; for the lower-protein diet, patients were offered 81 g of protein and 16.5×10^3 kJ (8.5% of energy from protein; protein-energy ratio, 5 mg/kJ per day) each day. In patients with edema, the higher-

protein diet was associated with prolonged anorexia, increased or persistent edema, and occasional instances of sudden death. Introduction of the lower-protein diet in December 1992 reduced these complications dramatically. This effect was so marked that subsequently, all patients with edema were given the low-protein diet during the initial phase of treatment. Data collected at the center have supported these observations, demonstrating a 4-fold reduction in mortality among patients with severe edema who received the low-protein diet.[10]

Data Collection and Coding

On admission, patients were registered and weighed and had their height measured by trained local enumerators, supervised by a specially trained nurse or the clinician responsible for collecting clinical data (S.C.). Body mass index was calculated from weight measurements taken within 2 days of admission; 97.6% (n=289) of BMIs were calculated on the day of admission. A rapid clinical screen, assessing degree of pitting edema, ascites, hydration, dysentery, diarrhea, anemia, signs of chest infection, and ability to stand, was performed by either the supervising clinician or a nurse. Weight and/or clinical condition of each patient was monitored daily. Outcome (death in the center, discharge alive, or lost to follow-up) was recorded on individual patient cards and in the center's register.

Data were transferred from inpatient record cards onto specially designed coding forms, double-entered into a personal computer, and validated for entry error. Pitting edema was coded using the classification of Beattie et al[11] (0=absent; 1=minimal edema on foot or ankle that is demonstrable but not visible; 2=visible on foot or ankle; 3=demonstrable up to knee; 4=demonstrable up to inguinal ligament; 5=anasarca). Pitting edema that was recorded as present but unquantified was assumed to be moderate (grade 3). Periorbital edema was coded as 1 (mild), 2 (moderate), or 3 (severe), with present but unquantified edema again assumed to be moderate (grade 2). Ascites was similarly coded. Severe edematous malnutrition was defined as either pitting edema greater than grade 2, periorbital edema greater than grade 1, or any ascites. Apparent dehydration was defined as sunken eyes, decreased urine output, or dry mucous membranes. Diarrhea (profuse, frequent, watery stool) and dysentery (profuse, frequent, watery stool with blood and with or without pus) were coded as present or absent. Missing data values were coded as not present.

The level of supervision of data collection was variable. Occasionally, expatriate access to the center by the supervising clinician and nurses was restricted for part of a day because of gun fighting, bandit attacks, attempts at hostage taking, and military occupations that occurred in Baidoa during the study period.

Data Analysis

Bivariate and multivariate logistic regression analyses were used to assess the association of clinical features at presentation with mortality in the center. Variables that were not independently associated with mortality were eliminated from the logistic models in a backward-stepwise fashion using estimation techniques. Odds ratios (ORs) of the 3 signs independently associated with death were used to construct a predictive model. If a patient exhibited none of these signs, the score was 0. If they exhibited 1 sign, their score was the OR associated with that sign. If more than 1 clinical sign was present, their score was the sum of the ORs associated with each sign. The sensitivity and specificity of predicted mortality at score intervals of 0.5 were calculated and receiver operating characteristic (ROC) curves were plotted. Receiver operating characteristic curves plot sensitivity against 100–specificity and are a useful means of assessing the ability of an indicator to discriminate between healthy and diseased persons or, in this case, between patients with differing outcomes (survival or death). A simpler model using a count of clinical signs was also constructed. In this model, the score for each patient was the number of 3 relevant clinical signs exhibited.

The association between BMI and survival was explored in a systematic manner. A series of indicator variables was created using successively higher BMI cut-points at intervals of 0.5 kg/m^2 (ie, variables were created to indicate whether an individual BMI was $<$10.0, 10.5, 11.0, 11.5, 12.0, 12.5, etc). Each indicator was tabulated against survival. The indicator with the most significant positive association (BMI $<$11.0 kg/m^2; OR, 2.44; 95% confidence interval, 1.11-5.32; Yates-corrected $\chi^2_1=5.22$; $P<.05$) was then included in the predictive model.

A simulation exercise was undertaken to validate the methods used to construct the models. Each run of the simulation involved splitting the data set into 2 parts by randomly selecting (using a pseudorandom number generator) approximately half of the available records as a training data set and using the other half of the data as a validation data set. The ORs and uncorrected χ^2 for each association between predictor variables and death were calculated using the training data set. Sums of ORs and sign-count models were then constructed using variables with significant positive associations with death, defined as any variable having an OR of greater than unity and an uncorrected χ^2 of greater than 3.84 (ie, $P\leq.05$ for tables with 1 *df*). Models constructed using these variables were then tested on the validation data set. The simulation was run 1000 times. All data entry and analyses were performed using Epi Info,[12] Logistic,[13] and Microsoft Excel.[14]

RESULTS

Ninety-one (23.8%) of the 383 patients died before discharge. Median time to death was 8 days (range, 1-53 days). TABLE 2 shows the clinical sign variables that were independently associated with survival and the ORs associated with these variables. Ascites was not associated with survival. Severe edema, inability to stand, and apparent dehydration were independently associated with mortality.

TABLE 3 presents the sensitivity and specificity for prediction of death in all 383 patients for all combinations of clinical models created using edema, inability to stand, and apparent dehydration. The most discriminatory model (ie, the model with the greatest sum of specificity and sensitivity) was that based on the presence of any 1 of these 3 signs. This model predicted 77% of deaths at a specificity of 59%.

FIGURE 1 shows the ROC curves for the prediction of short-term mortality using the sum-of-ORs clinical model and BMI. The prediction of death by the sum of the ORs of severe edema, inability to stand, and apparent dehydration performed at the highest level of sensitivity and specificity. Prediction of death using BMI alone in these patients yielded worse-than-random results. When BMI was used in a subpopulation selected to include only marasmic patients who could stand (n=218), performance was similar to the clinical model, predicting 46% of deaths at a specificity of 85%. When use of BMI was further restricted to include only marasmic women who could stand (n=108), BMI performed better than the clinical model, predicting 56% of deaths at a specificity of 87%.

The ROC curve for the model constructed by counting clinical signs was identical to that produced using the sum-of-ORs clinical model. Addition of a BMI marginally improved these models. ROC curves for these models are presented in FIGURE 2.

Nine hundred ninety-three runs (99.3%) of the simulation of the sum-of-ORs clinical model yielded a predictive model better than random. The mean area under the ROC curves for these 1000 simulations was 63.25% (SD, 4.39%). Nine hundred ninety-seven runs (99.7%) of the sign-count clinical model and BMI yielded a predictive model better than random. The mean area under the ROC curves for these 1000 simulations was 63.42% (SD, 4.23%).

COMMENT

The risks of mortality associated with apparent dehydration, inability to stand, and severe edema were independent of each other. A patient presenting with more than 1 of these signs therefore had a risk of mortality equivalent to the sum of the risks of all the signs that were present. A scoring system based on the sum of the ORs predicted 77% of deaths at a specificity of 59%. A simplified model, using only the presence or absence of 3 clinical signs—severe edema, inability to stand, and apparent dehydration—predicted deaths in a near identical fashion (Figure 2). Use of this sign-count model required only a count of relevant clinical signs, not calculation of ORs, which would be difficult in the field. Eliciting the 3 clinical signs used in the model was quick and easy in all patients and required no equipment. Consequently, the sign-count model can be readily taught to local workers and is suitable for use as a prognostic model in the field, even during the early phases of a famine relief program.

The capacity of BMI to predict death was limited. Only among female marasmic patients who could stand did BMI perform better than the clinical

Table 2. Clinical Signs Associated With Survival in Severe Malnutrition (N = 383)

Variables	Survivors, % (n = 292)	Nonsurvivors, % (n = 91)	Unadjusted Odds Ratio (95% Confidence Interval)
Inability to stand	7	19	2.96 (1.40-6.26)
Dehydration	22	43	2.73 (1.60-4.66)
Severe edema	19	36	2.45 (1.41-4.27)
Dysentery	29	38	1.50 (0.88-2.53)
Anemia	21	25	1.28 (0.71-2.31)
Diarrhea	34	37	1.18 (0.70-1.99)
Chest infection	58	57	0.97 (0.58-1.61)

Table 3. Prediction of Mortality by 3 Clinical Signs (N = 383)*

Signs	No. of Nonsurvivors Predicted to Die	No. of Survivors Predicted to Die	Sensitivity, %	Specificity, %	Accuracy, %	PPV, %	NPV, %
Single							
Dehydration	39	63	43	78	70	38	81
Edema	33	55	36	81	70	38	80
Inability to stand	17	21	19	93	75	45	79
Combined using "and"							
Edema and inability to stand	3	3	3	99	76	50	77
Dehydration and inability to stand	8	4	9	99	77	67	78
Dehydration and edema	9	12	10	96	75	43	77
All 3 signs	1	1	1	100	76	50	76
Combined using "or"							
Edema or inability to stand	47	73	52	75	69	39	83
Dehydration or inability to stand	48	80	53	73	68	38	83
Dehydration or edema	63	106	69	64	65	37	87
Any 1 sign	70	121	77	59	63	37	89
Any 2 signs	18	17	20	94	77	51	79

*PPV indicates positive predictive value; NPV, negative predictive value.

models. When nonmarasmic patients and those unable to stand were included (ie, the entire patient cohort), the prediction of mortality using BMI was worse than random (Figure 1). Assessment of BMI was also difficult and time-consuming. Dehydration present among patients admitted to the center reduced admission BMIs. Because apparent dehydration was also a sign of poor prognosis, its presence tended to make BMI a better predictor of death in the center. The inability of most severely dehydrated people to stand meant that they could not have their BMI estimated within 2 days of admission and were therefore not included in the BMI prognostic models. It is therefore likely that the reduction of admission BMIs due to dehydration was not a major effect.

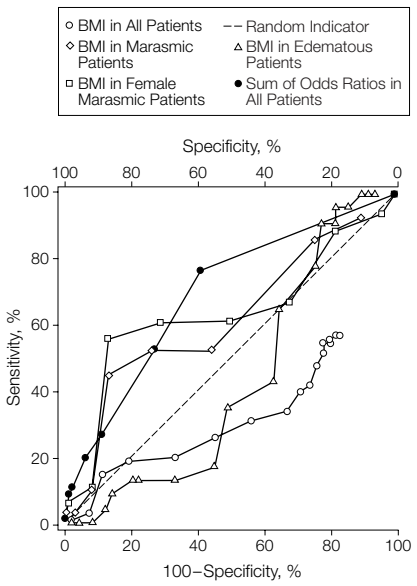
Presence of severe edema was associated with a poor prognosis and increased admission BMI. This confounding meant that the ability of BMI to predict death among patients with edema was worse than random. Because severe edema was common, BMI was not useful as a prognostic indicator when applied to the entire center population (Figure 1).

These results indicate that at the extremes of emaciation observed in adult therapeutic feeding centers, clinical illness is a better indicator of prognosis than degree of wasting as defined by BMI. A model using the presence of readily discernible clinical signs is useful in identifying patients at high risk of death. The high-risk patients identified by this prognostic model can then be moved to specialized feeding centers or areas within existing feeding centers with the most motivated staff, a higher level of medical supervision, and, if necessary, higher caregiver-patient ratios. This is a different role than that of screening admissions for entry into feeding centers, a research priority in severe adult/adolescent malnutrition.[15] Rather than identifying inpatients with a poor prognosis, a screening indicator must identify persons in the general population who are likely to respond to treatment if admitted to a feeding center but who will die if not admitted. The specificity and sensitivity requirements for screening are different than those required for prognostic indicators. To be useful in famine relief programs, where there are often large crowds of people attempting to gain entry into feeding centers, a screening indicator must have a high specificity. This is not the prime requirement for a prognostic indicator. We have demonstrated that the sign-count model is sensitive for predicting death within a therapeutic feeding center. We have not assessed its potential for use as a screening tool to exclude individuals from admission to feeding centers.

This potential use for screening admissions to therapeutic feeding centers needs to be investigated further. Although the model is somewhat nonspecific for identification of patients who would die despite having been given treatment in the center, it is likely that in the absence of treatment, many more of the individuals identified would have died. The model might therefore be more specific if used for screening. To increase the model's specificity for identifying malnourished individuals at greater risk of dying, an indicator of nutritional status would need to be added to the model. Middle upper arm circumference (MUAC), recently shown to be a potentially useful indicator of acute adult malnutrition,[16] might be suitable. Addition of MUAC would differentiate between those with clinical illness but no malnutrition, who would be better treated in medical units, from those with both illness and malnutrition, who would be best treated in specialized feeding centers. By weighting the model appropriately, having an MUAC below a certain threshold could be made a necessary prerequisite for selection. This would ensure a high prevalence of malnutrition in the population assessed by the sign-count part of the model.

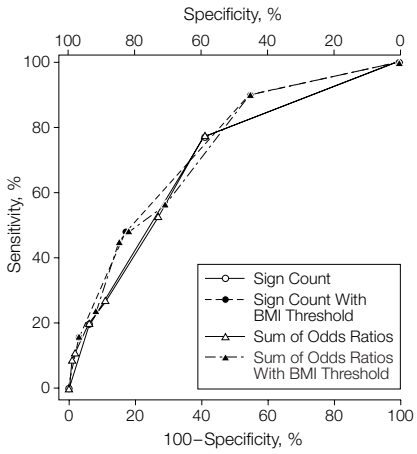
Within this selected population, the specificity of the clinical signs for identifying death among persons who did not receive treatment would be high, fulfilling the requirement for screening. Use of this single model would be equivalent to application of a 2-stage screening procedure. Such a 2-stage system is similar to that used by 1 of us (S.C.) when confronted with large crowds of malnourished adults. In such situations, a rapid visual inspection and a very brief clinical examination are undertaken to assess fat in the upper arms out-

Figure 1. Receiver Operating Characteristic Curves for Prediction of Mortality by the Sum of Odds Ratios for 3 Clinical Signs and Body Mass Index (BMI)



The 3 clinical signs are severe edema, inability to stand, and apparent dehydration.

Figure 2. Prediction of Short-term Mortality by Counting 3 Clinical Signs With and Without a BMI Threshold



The 3 clinical signs are severe edema, inability to stand, and apparent dehydration. A body mass index (BMI) threshold of 11.5 kg/m^2 or less was used.

side of the center, followed by more involved anthropometric and clinical inspection inside the center. In this ad hoc system, the initial screen outside of the center increases the prevalence of severe malnutrition requiring urgent assistance among persons who are allowed through the gates to be assessed by a more time-consuming clinical examination. In this selected population, the higher prevalence of life-threatening malnutrition makes the relatively low specificity of the clinical screen less important. The sign-count model proposed here, combined with an MUAC cutoff, would formalize this method, making it more useful to workers with less experience. The threshold of both MUAC and the clinical score chosen as a screening cutoff would depend on the context and the relative balance of resources and needs.[17]

Emergency relief programs must ensure that the majority of a population has access to the minimum requirement to maintain life. This requires prioritizing lower-input interventions with a large coverage of the vulnerable population above high-input services treating relatively few. Access to a life-sustaining general ration, providing at least 8786 kJ from grains, legumes, and vegetable oil; adequate water; sanitation; basic health care; and dry supplementary feeding, must, therefore, form the basis of any relief program.[18] Therapeutic feeding centers are efficient and effective only if these basic prerequisites are in place. This hierarchy of interventions constitutes a form of triage. During the initial stages of famine, need will usually outstrip the available resources and the focus should be on ensuring that the general ration is adequate before targeted feeding centers are established. At this stage, those too malnourished to survive with this basic support will die. As resources increase, it will become possible to undertake therapeutic feeding, although, initially, clinical triage may be necessary.

For example, in the town of Wau in southern Sudan during June through August 1998, more than 100 therapeutic centers would have been required to treat the estimated 16 000 children and adults requiring therapeutic feeding.[19] At that time, there was only a single 24-hour therapeutic feeding center with a maximum capacity of 400 patients. In this context, given the limited means available, selecting only those patients with a good chance of survival would have optimized the efficient use of resources. In this study, the combination of 2 relevant clinical signs predicted death at sensitivities of greater than 95%. In Wau, the combination of these 2 signs would have been a useful triage tool to determine the low end of the spectrum of malnutrition severity among patients whom the center would admit.

Relief programs are rarely totally overwhelmed, and it is important that the existence of a triage tool does not undermine international will to provide sufficient humanitarian assistance during emergencies. Screening and prognostic indicators are also different than markers of improvement during treatment. In this study, maintenance of fluid balance and hydration, disappearance of edema, and a steady increase in weight in the absence of increasing edema were all markers of improvement. This has been reported previously.[10,20]

Ideally, a study evaluating the relationship between clinical signs and risk of mortality in a general population experiencing famine is required to establish relevant clinical screening criteria. However, conducting such broad-based population studies is probably not feasible during famine and none have yet been undertaken in such conditions. Given these difficulties, evaluating prognostic models in selected feeding center populations is a feasible alternative. It is certainly better than the current absence of information on prognostic indicators in famine.

In conclusion, counting simple clinical signs is a useful method of assessing prognosis in severe adult and adolescent malnutrition during famine. The addition of an anthropometric indicator is likely to make these models useful for screening admissions of adults to feeding centers. The poor association of BMI with prognosis and difficulties in obtaining BMI estimations during extreme conditions, such as the famine in Somalia, make BMI inappropriate for such a role. Middle upper arm circumference might prove to be more useful in this context. More work on identifying relevant clinical signs and combining them with MUAC in such models for use in screening is required.

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