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(Accepted 13 July 1993)

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Serum albumin concentration, arm circumference, and oedema and subsequent risk of dying in children in central Africa

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Abstract

Objective—To measure the prognostic value of clinical, anthropometric, and biological indicators of protein energy malnutrition in hospitalised children.

Design—Hospital based follow up study from admission to discharge or death of a cohort of children.

Setting—Paediatric hospital in Zaire.

Subjects—1129 children consecutively admitted between August 1986 and October 1988.

Main outcome measures—Height, weight, arm circumference, skinfold thicknesses, serum albumin concentration, and mortality.

Results—Mortality was higher in wasted children and in those with a mid-upper arm circumference <125 mm, a serum albumin concentration <16 g/l, and oedema. After multivariate analysis, serum albumin concentration was the best predictor of subsequent risk of dying. Mid-upper arm circumference and oedema, however, still contributed considerably to evaluation of mortality.

Conclusions—In this specific environment of central Africa an isolated clinical sign such as oedema is not enough to detect children with a high risk of dying among those admitted to paediatric wards with severe protein energy malnutrition. Measurement of additional indicators such as arm circumference and serum albumin concentration seems to be of crucial importance.

Introduction

In developing countries protein energy malnutrition is common among children admitted to hospital and is associated with a high morbidity and mortality.¹⁻⁴ A nutritional assessment is mandatory to treat and follow these severely ill patients. Different anthropometric and biological variables have been proposed, biometry being the most commonly used tool. Major signs looked for are oedema and muscle wastage, isolated or in combination.

Most common classifications of protein energy malnutrition are usually based on weight loss compared with international reference data and the presence of oedema, which enables differentiation of kwashiorkor

from marasmus.⁵ Different authors have found a close association between some anthropometric measurements and the risk of dying during the hospital stay.⁶⁻⁷ In the oedematous form of protein energy malnutrition, however, there is no simple association between mortality and the severity of weight loss, whereas the albumin concentration at admission is strongly associated with mortality.⁸

In central Africa all forms of protein energy malnutrition are often encountered, particularly in hospitals. Our aim was to detect from various anthropometric measurements, clinical signs, and biochemical indices very commonly performed or collected those mainly associated from the time of admission with a higher risk of dying.

Our purpose was to identify the most discriminant and predictive of these markers.

Patients and methods

The children's hospital of Lwiro is located in south Kivu in Zaire, at the eastern border of the country. In these highlands most people are living by subsistence farming, and their food supply is low in energy and protein with large seasonal variations.

Between August 1986 and October 1988 1129 children admitted consecutively to the paediatric hospital of Lwiro were included in the follow up study; two thirds of the children suffered from clinical protein energy malnutrition.

We analysed different variables at baseline and their association with subsequent mortality. The median age of the children was 27 months; three quarters were aged under 5 years and nearly half under 2 years. The average duration of admission to hospital was 26 days, but nearly half of the children had left the hospital within two weeks. At the time of admission 395 children suffered from gastroenteritis and 203 were dehydrated; moreover 350 had a body temperature above 37.5°C, 237 had an infection of the lower respiratory tract, and 304 had malaria.

We studied the anthropometric indicators of height for age, weight for height, mid-upper arm circumference, and tricipital and subscapular skinfold thicknesses. Weight was measured to the nearest 10 g. Weight scales were calibrated daily. Recumbent length

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BMJ 1993;307:710-3

or standing height were measured to the nearest 1 mm and 2 mm, respectively. Arm circumference was measured with a plastic tape to the nearest millimetre. Skinfold thicknesses were measured in the upright position with Harpenden callipers. According to the Waterlow classification children were classified in four groups of height and weight.^{9 10} They were classified for arm circumference according to cut off points of < 115 mm, 115-124 mm, 125-134 mm, and $\geq$ 135 mm. Children were also classified according to the quarters of the distribution of tricipital and subscapular skinfold thicknesses.

In addition, we considered in the analyses the presence of oedema and serum albumin concentration. The presence of oedema was determined by applying pressure for 30 s to the pretibial region. Serum albumin concentration was determined according to the technique of Sonnet and Rodhain.¹¹ For subsequent analyses serum albumin concentrations were categorised into four groups (< 16 g/l, 16-22 g/l, 23-29 g/l, and $\geq$ 30 g/l).

As we aimed to establish early detection of accurate predictors of mortality all data collected at baseline were considered, notwithstanding the presence or absence of oedema or a possible degree of dehydration. Continuous variables were categorised to obtain estimates of their effects on mortality that are easy to interpret; for arm circumference and serum albumin concentration usual cut off points were used.

Statistical analysis was performed by using the SPSS 4.0 release for Unix and the biomedical programs data package.^{12 13} Survival at 60 days was the end point considered; cumulative mortality (proportion of deaths at 60 days) was obtained in each category of indicators. To measure the strength of the association between these indicators and subsequent risk of dying we computed relative risks and their 95% confidence intervals. The χ^2 test was used in the analysis of contingency tables. Finally, logistic regression was applied by using a backward elimination procedure. Because data were missing in 174 subjects on admission, the sample on which logistic regression could be applied was reduced from 1129 to 955 subjects. Age, categorised into four groups (< 12 months, 12-23

months, 24 months to < 5 years, and $\geq$ 5 years) was also included in the multivariate analyses as a potential confounder. With the variables selected from the first logistic regression new models were built including the interactions between any two of the three variables (arm circumference, serum albumin, and oedema). Because of the small number of subjects in some cells the categories of serum albumin concentration and arm circumference had to be grouped together to include interactions in the model. The interactions were tested by subtracting the log likelihood statistics of the models with and without the interactions terms. In a further analysis, each interaction was eliminated with a backward procedure based on the Wald test. Odds ratios and their 95% confidence intervals were estimated from the final logistic model.¹⁴⁻¹⁷ The coefficients of this logistic equation were used as weights to compute a prognostic index for each subject. Survival curves (Kaplan-Meier curves combined with Breslow test) were estimated in four groups of subjects classified according to their value of the prognostic index. To form the groups quarters of the distribution of the prognostic index were considered; since survival was similar in the two lowest quarters, representing low risk subjects, these two groups were combined into one group. The fourth quarter was divided in two groups: the first one contained 15% of the total distribution (from 76% to 90%) and the second one the last 10% of the total distribution (from 91% to 100%). The purpose of that subdivision was aimed at isolating patients at highest risk. Finally, validation of the resulting logistic model was performed by using the data from the children admitted during the years 1989 to 1991.

Results

The distributions of the indicators of protein energy malnutrition illustrate the poor nutritional condition of the children admitted at Lwiro (table I). With early deaths taken into account, 197 subjects died in hospital, which gives a figure of 17.4% or a death rate of two per 100 children months.

The cumulative mortality varied with respect to each indicator and was especially high among children admitted with serum albumin concentrations lower than 16 g/l, with arm circumference under 115 mm, or subscapular skinfold thickness under 4 mm (table I). The proportion of deaths in the four age groups (table I) did not differ significantly. The logistic regression model was constructed with all anthropometric variables and age. Age was associated with serum albumin concentration and arm circumference. In children aged < 1 year we observed the highest mean serum albumin concentration and, not unexpectedly, the lowest proportion of children with serum albumin concentration < 16 g/l (table II). Mean arm circumference increased significantly with age; arm circumference was < 115 mm in about a third of the children under 1 year (table II). Among the anthropometric variables introduced in the multivariate analysis arm circumference was the only one to have a significant effect on mortality. In the logistic regression model taking arm circumference, serum albumin concentration, oedema, and age into account (table III), however, serum albumin concentration seemed to have the strongest effect on mortality. Oedema also contributed significantly to the model but to a lesser degree than the two other nutritional markers considered. When the model included both serum albumin concentration and age, age became significant. Inclusion of age produced a moderate reduction of odds ratios for arm circumference and a slight increase of odds ratios for serum albumin concentration.

Stratified analysis indicated that the risk of death in

TABLE I—Distribution of subjects, cumulative mortality at 60 days, and relative risk (95% confidence interval) in each category of anthropometric variables, serum albumin concentration, oedema, and age for the children admitted to hospital in Lwiro between August 1986 and October 1988

Variable	Distribution (No (%))	Cumulative mortality (No (%))	Relative risk (95% confidence interval)
Waterlow classification (n=959)			
Wasted and stunted	180 (18.8)	50 (27.8)	4.3 (2.6 to 7.0)
Stunted	400 (41.7)	60 (15.0)	2.3 (1.4 to 3.8)
Wasted	87 (9.1)	14 (16.1)	2.5 (1.3 to 4.7)
Normal	292 (30.4)	19 (6.5)	1.0
Arm circumference (mm) (n=1043):			
< 115	175 (16.8)	57 (32.6)	3.7 (2.6 to 5.3)
115-124	159 (15.2)	33 (20.8)	2.4 (1.6 to 3.6)
125-134	211 (20.2)	28 (13.3)	1.5 (0.9 to 2.4)
$\geq$ 135	498 (47.8)	44 (8.8)	1.0
Triceps skinfold thickness (mm) (n=1041):			
$\leq$ 5	256 (24.6)	51 (19.9)	2.0 (1.3 to 3.0)
6-7	352 (33.8)	58 (16.5)	1.6 (1.1 to 2.5)
8	158 (15.2)	24 (15.2)	1.5 (0.9 to 2.5)
$\geq$ 9	275 (26.4)	28 (10.2)	1.0
Subscapular skinfold thickness (mm) (n=1041):			
$\leq$ 3	196 (18.8)	62 (31.6)	4.5 (2.9 to 6.9)
4	247 (23.7)	44 (17.8)	2.5 (1.6 to 4.0)
5	229 (22.0)	31 (13.5)	1.9 (1.2 to 3.2)
$\geq$ 6	369 (35.4)	26 (7.0)	1.0
Serum albumin (g/l) (n=1022):			
< 16	214 (20.9)	87 (40.7)	10.6 (5.5 to 20.5)
16-22	256 (25.1)	38 (14.8)	3.9 (1.9 to 7.8)
23-29	318 (31.1)	27 (8.5)	2.2 (1.1 to 4.6)
$\geq$ 30	234 (22.9)	9 (3.8)	1.0
Oedema (n=1106):			
Present	320 (28.9)	102 (31.9)	3.1 (2.4 to 4.0)
Absent	786 (71.1)	81 (10.3)	1.0
Age (years) (n=1100):			
< 1	302 (27.5)	53 (17.5)	1.2 (0.8 to 1.8)
1 to 22	197 (17.9)	28 (14.2)	1.0 (0.6 to 1.5)
2 to 5	325 (29.5)	63 (19.4)	1.3 (0.9 to 1.9)
$\geq$ 5	276 (25.1)	40 (14.5)	1.0

TABLE II—Mean (SD) serum albumin concentrations and arm circumferences and numbers (percentages) with concentration <16 g/l and circumference <115 mm by age group

Age (years)	Serum albumin (g/l)			Arm circumference (mm)		
	No	Mean (SD)	No (%)	No	Mean (SD)	No (%)
<1	264	28 (7)	10 (4)	276	122 (19)	86 (31)
1 to <2	184	25 (8)	20 (11)	184	128 (16)	31 (17)
2 to <5	307	21 (8)	110 (35)	318	132 (15)	40 (12)
≥5	253	22 (9)	73 (28)	253	148 (26)	18 (7)

TABLE III—Logistic regression model including arm circumference, age, serum albumin concentration, and oedema (147 dead, 808 discharged)

Variables	Odds ratio (95% confidence interval)	p Value
Serum albumin (g/l):		
<16	12.49 (5.06 to 30.82)	<0.001
16-22	3.43 (1.48 to 7.91)	<0.001
23-29	1.81 (0.79 to 4.12)	0.159
≥30	1.00	
Arm circumference (mm):		
<115	4.76 (2.76 to 8.21)	<0.001
115-124	2.51 (1.40 to 4.51)	0.002
125-134	1.25 (0.69 to 2.25)	0.466
≥135	1.00	
Oedema:		
Presence	2.83 (1.65 to 4.85)	<0.001
Absence	1.00	
Age (years):		
<1	2.60 (1.29 to 5.26)	0.008
1 to <2	1.33 (0.66 to 2.69)	0.428
2 to <5	0.95 (0.55 to 1.64)	0.851
≥5	1.00	

children with arm circumference <115 mm relative to children with arm circumference ≥125 mm was lower when the serum albumin concentration was <16 g/l than when it was ≥23 g/l and that the relative risk associated with arm circumference was lower in the presence of oedema. In the logistic model, however, none of the interactions between the analysed indicators was significant. A prognostic index was derived from the logistic model (table III); high values of this index were associated with lower values of arm circumference, serum albumin concentration, and age and with the presence of oedema.

The figure shows the important decrease in the survival rates when the values of the prognostic index are high. The difference between survival rates for the subjects with low values of the prognostic index versus those with the highest values reached 25% at one week from admission and 40% at two weeks.

Discussion

In Africa mortality in patients admitted to hospital in a state of severe protein energy malnutrition with or

TABLE IV—Logistic regression model including arm circumference, age, serum albumin, and oedema obtained in validation set (admissions from 1989 to 1991: 158 dead, 1238 discharged)

Variables	No	Odds ratio (95% confidence interval)	p Value
Serum albumin (g/l):			
<16	169	6.46 (3.32 to 12.57)	<0.001
16-22	313	3.18 (1.77 to 5.71)	<0.001
23-29	513	1.34 (0.76 to 2.37)	0.317
≥30	401	1.00	
Arm circumference (mm):			
<115	208	3.03 (1.84 to 4.98)	<0.001
115-124	229	1.94 (1.16 to 3.24)	0.011
125-134	354	1.36 (0.83 to 2.24)	0.219
≥135	605	1.00	
Oedema:			
Presence	297	1.91 (1.20 to 3.02)	<0.006
Absence	1099	1.00	
Age (years):			
<1	464	2.47 (1.30 to 4.69)	0.006
1 to <2	266	2.04 (1.07 to 3.89)	0.030
2 to <5	420	1.30 (0.71 to 2.37)	0.396
≥5	246	1.00	

without oedema ranges from 9% to 30%.^{1-3,8,18} Several studies have clarified the association between anthropometric indicators and hospital mortality.^{14,6} In Kivu province cumulative mortality is twice as high for wasted and stunted children when compared with their counterparts. Weight, however, is a difficult variable to interpret in malnourished patients. It depends on total body water content, the proportion of which is said to be abnormally high in malnourished children¹⁹ or abnormally low in dehydrated children.

More recently Briend *et al* have shown the importance of measurements of the arm circumference to predict death among children admitted for diarrhoeal disease.⁷ The arm circumference is a good indicator of the muscle mass,²⁰ and muscle mass may be a major determinant of survival in prolonged under-nutrition.^{21,22} In Kivu we found mortality in children with an arm circumference <115 mm to be 3.7 times higher than in those with an arm circumference ≥135 mm. These results confirm the importance of measuring the arm circumference in the prediction of risk of death in hospital, especially as this measurement is easy to perform. Nevertheless, the arm circumference can be influenced by the fat panniculus or the presence of oedema,²³ two common conditions in children admitted to hospital in central Africa.

Though most quoted studies consider only anthropometric variables several investigations have analysed the presence or absence of oedema at the time of

Survival curves during first 60 days of hospital admission (see text). Curve 1 (n=473): low risk children, first two quarters (1-50%) of prognostic index distribution. Curve 2 (n=245): medium risk children, third quarter (51-75%) of prognostic index distribution. Curve 3 (n=145) and curve 4 (n=87): fourth quarter (76-100%) of prognostic index distribution, divided in larger group containing subjects from 76% to 90% (curve 3) of distribution and smaller group from 91% to 100% (curve 4), corresponding to upper tenth of distribution and referring to subjects at highest risk. Curves differ significantly (p<0.001).

admission. In Mexico a univariate analysis could not prove any significant association between the presence (or absence) of oedema and mortality among admitted patients.⁶ In Dakar, on the contrary, multivariate analysis disclosed a relative risk reaching 6.2.² In Kivu the relative risk of mortality for children with oedema compared with those without is only about 3.

The circulating concentration of transport proteins, traditionally albumin, has been used to define protein deficiency in clinical practice.^{24,25} This indicator of protein shortage is also associated with a higher risk of death in hospital; in children admitted to hospital with oedematous malnutrition the serum albumin concentration at admission was closely related to the mortality.⁸ Our findings suggest that in the Kivu region the same association that is valid for the oedematous children is also found among all the admitted children. Indeed, the highest relative risk recorded (10.6) corresponded to the group of children

admitted with an albumin concentration <16 g/l as opposed to those admitted with an albumin concentration ≥ 30 g/l. Furthermore, as albumin concentration is independent of the variation in oedema its determination is already relevant on admission.²⁶ This variable, however, is not specific for protein deficiency as many other factors such as energy deficiency, zinc deficiency, infections, and liver disease are just as likely to be the cause of an observed low concentration of transport proteins as is protein deficiency.²⁷

In healthy children serum albumin concentration does not vary much with age between 3 months and 5 years; in our data we observed on average higher serum albumin concentrations in very young children (<1 year) and lower concentrations in children between 2 and 5 years of age. This pattern can be explained by the characteristics of kwashiorkor itself, for which the peak incidence occurs at about 2 years, corresponding to weaning.²⁸ Similar results have been found in Uganda.²⁹ In Kivu in the multivariate analysis the serum albumin concentration seemed to have the dominant impact on mortality, although arm circumference and oedema remained important. This model has been verified on data collected from 1989 to 1991; all three indicators considered still had a significant effect on mortality (table IV), although the estimated odds ratios were lower than those observed in the present investigation (table III). This may result from the great variability in the characteristics of the admitted children and the various reasons for their admission. No significant interactions between serum albumin concentration, arm circumference, and oedema were detected in the logistic analysis.

We conclude from this work that in this relatively specific socioeconomic and nutritional environment of central Africa the recording of clinical symptoms such as oedema in hospital is not enough to detect reliably those children most likely to die, even though the symptom is significantly associated with hospital mortality. The measurements of the arm circumference, an indicator of the lean body mass, and the concentration of transport proteins such as the serum albumin seem to be crucial and complementary. It would be interesting to determine whether these criteria would be of the same relevance in outpatients living in the same region or among inpatients living in other regions.

This work was supported by a grant from the Fonds National de la Recherche Scientifique (number 3.4532.86). We also thank the Fondation Universitaire David et Alice Van Buuren.

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Clinical implications

- In developing countries protein energy malnutrition in children admitted to hospital contributes to a high case fatality rate
- Anthropometric measurements alone may not predict which children have a high risk of dying
- In this study death was more common among wasted children (stunted or not) and those with a mid-upper arm circumference smaller than 125 mm, a serum albumin concentration lower than 16 g/l, and oedema
- Serum albumin concentration was the best single predictor of subsequent risk of dying
- In central Africa combined anthropometric measurements and biology with clinical symptom are useful predictors of death
- In central Africa both physical measurements and physiological variables need to be considered to detect which malnourished children are at risk of dying

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(Accepted 2 July 1993)