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RESEARCH

Pre-albumin as a marker for predicting weight loss in hospitalised children

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Objectives: This study sought to determine the diagnostic utility of serum pre-albumin in predicting weight loss in hospitalised children.
Design: A hospital-based longitudinal survey was carried out between December 2013 and February 2014.
Setting: Aga Khan University Hospital, Nairobi, Kenya, a tertiary care hospital.
Subjects: A total of 170 children aged 29 days to 15 years who met the inclusion criteria were included in the study.
Outcome measures: Serum pre-albumin levels and weight were measured at admission and repeated after 48–96 h. Sensitivity, specificity, and positive and negative predictive values were calculated to determine the diagnostic utility of serum pre-albumin in predicting weight loss in hospitalised children.
Results: Of the 170 children studied, 57% and 60% had a drop in serum pre-albumin level and weight within the first four days of hospitalisation respectively. A drop in pre-albumin occurred in 68% of the 103 patients who had weight loss ($p < 0.001$). Using a serum pre-albumin cut off point of < 0.15 g/l at admission, sensitivity and specificity of serum pre-albumin in predicting weight loss were 76.7% and 29.0% (negative predictive value = 42.9%; positive predictive value = 64.2%). Positive and negative likelihood ratios were low at 1.08 and 0.8. The majority of the patients (72.3%) were already at risk of malnutrition as determined by the pre-albumin risk stratification on admission.
Conclusion: Serum pre-albumin is not an accurate surrogate for weight loss during hospitalisation. It is, however, useful in identifying patients at risk of malnutrition on admission and during hospitalisation.

Keywords: hospital malnutrition, weight loss, serum pre-albumin

Introduction

Malnutrition among hospitalised children occurs as a result of reduction in food intake, increased dietary losses and increased calorie requirement as a result of disease-induced high catabolic state.[1] A child's nutritional status often deteriorates after admission to hospital;[1–7] it occurs worldwide and affects patients of all ages.[5] Researchers have reported a correlation between 'hospital-acquired' malnutrition and the length of hospital stay, which in turn is associated with clinical deterioration and increased risk of complications, and increased use of hospital resources.[3,4] There is, therefore, a need for health facilities to adopt a minimum set of tools for evaluating the nutritional status and to plan for its management in hospitalised children.

Although anthropometry is the most commonly used indicator for evaluating nutritional status and is generally considered to be a basic requirement of the admission process, it may be inappropriate for detecting acute nutritional changes over a short period;[8] this could, for example, be the case in patients with dehydration or fluid accumulation. Moreover, many limitations exist within clinical practice including a lack of functioning and well-calibrated equipment and a lack of standardisation in recording of measurements.[2] A biochemical nutritional marker with a short biological half-life, able to predict catabolic rate, that changes readily in response to protein intake and is uninfluenced by pathological processes would be a more sensitive surrogate predictor of acute weight loss.[8,9] Biochemical markers that come close to meeting this requirement include serum albumin and pre-albumin.

Although serum albumin level has historically been used to determine nutritional status, it is relatively insensitive to acute changes in nutrition. This is because of its long half-life of 14–20 days and its presence in a relatively large body pool besides being redistributed between the body's vascular and interstitial spaces under various physiological conditions.[10] Albumin levels typically take about 14 days to normalise after depletion of the entire body pool when appropriate nutrition is initiated.[9,11] Serum albumin is a relatively late marker thus rendering it inappropriate for assessment of changes in nutritional status during a brief hospitalisation.

Serum pre-albumin, a precursor of albumin, has been proposed as a more suitable marker for measuring rapid changes in nutritional status compared with albumin.[9,11] It is easily measurable and, unlike other serum proteins, is less affected by liver disease.[9,11] Although pre-albumin is produced primarily by the liver, its production is maintained until late in liver pathology.[9,12] It is also produced by pancreatic islet cells within the embryonic yolk sac, choroid plexus, and by enterochromaffin cells in the gastrointestinal mucosa. Compared with other proteins in the body, pre-albumin is also considered a unique marker for protein synthesis due to its high essential to nonessential amino acid ratio.[9,11] Unlike albumin, pre-albumin is unaffected by hydration[9,13] and has a shorter half-life (2–4 days), therefore its level reflects recent dietary intake.[14] Studies have shown that measurement of serum pre-albumin levels enables early recognition of acute malnutrition, before weight changes occur.[9,13] Within four to eight days of starting nutritional supplementation pre-albumin levels are expected to rise, with a target increase of 2 mg/dl per day and a return to normal levels within eight days, which suggests adequate nutritional support. However, levels rising by less than 4 mg/dl in eight days indicate a poor prognosis and the need for intense enteral or parenteral nutritional support.[9]

Despite serum pre-albumin being considered a sensitive nutritional marker for some time, there are limited data on its

utility in children. This study investigated the diagnostic utility of serum pre-albumin in predicting weight loss among hospitalised children.

Methods

A longitudinal survey was carried out at the Aga Khan University Hospital, Nairobi (AKUH,N), a 254-bed private tertiary institution. The paediatric ward is a 30-bed-capacity unit, comprising a five-bed paediatric high dependency unit and 25 general ward beds. The paediatric ward admits an average of 1 300 patients annually. The hospital largely serves Nairobi's population but also receives referrals from other parts of the country and the wider Eastern African region.

Children aged between 29 days and 15 years and who were admitted for ≥ 48 h were eligible for inclusion. Those with oedematous malnutrition (presence of bilateral pitting oedema of nutritional origin) were, however, excluded. Informed written consent was obtained from parents or accompanying guardians before enlisting patients. Ethical approval for the study was obtained from the Aga Khan University Ethics Committee (Ref: 2013/REC-39/v4, 09/12/2013).

The principal investigator or an assistant trained in taking anthropometric measurements took all the weights at admission and discharge using a Seca® (Birmingham, United Kingdom) digital baby-weighing scale for children less than 15 kg body weight, measured to the nearest 10 g. A Seca® (United Kingdom) standing weighing scale was used for children above 15 kg body weight and subjects were measured to the nearest 100 g. The two weighing scales were exclusively used to take weight for all the children. Participants were weighed undressed if < 2 years and with minimal clothing (undergarment) for those above two years. In the case of dehydration, weight was repeated after adequate rehydration (defined using WHO criteria: child being alert, normal skin turgor, moist mucous membranes, flat anterior fontanel, eyes not sunken, warm extremities, capillary refill ≤ 2sec) and considered as the baseline. Assessment for re-hydration was done by the attending clinician. Weight was taken daily under the same conditions (early in the morning, after voiding and before feeding).

Blood samples (2 ml each) for serum pre-albumin were taken at admission and between 48 and 96 h post-admission. These were done during routine sampling where applicable to minimise patient discomfort. Samples were labelled with the serial number of the patients and transported in a biohazard bag immediately after collection to the Aga Khan University Hospital, Nairobi laboratory where they were centrifuged, and the serum stored at –20 °C. The pre-albumin was measured using a commercially available, Cobas C Integra Pre-albumin Kit (Roche Diagnostics, Mannheim, Germany) with capacity to run 100 samples at a time. All the samples were analysed after completion of data collection to avoid wastage of pre-albumin kits. The assays were all performed by one technician who strictly followed the manufacturer's protocol.

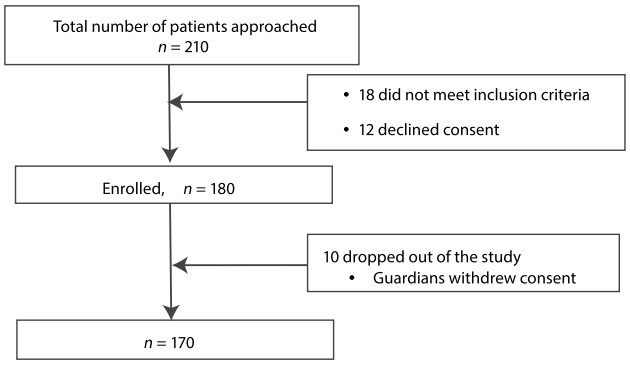

Figure 1: Flow chart of recruitment process.

All children who were admitted to the hospital underwent routine nutritional assessment and received an appropriate diet plan recommended by the hospital's nutritionist. The clinical team was informed of any children found to be malnourished based on anthropometry taken on admission. All patients were followed up till the point of discharge or death.

Demographic data and laboratory results of each patient were stored in a database using a Microsoft Excel® (Microsoft Corp, Redmond, WA, USA) database using a unique serial number as its identifier, so as to maintain patient anonymity. Data were regularly backed up both on- and off-site. Access to the results was restricted to the principal investigator and respective co-investigators.

Data were collected from December 2013 to February 2014 and were analysed using Stata data and statistical software (Stata 11.0®; StataCorp, College Station, TX, USA). Categorical data were analysed using proportions and continuous data were analysed using means, medians, standard deviation and interquartile range.

For the purpose of this study, weight loss was defined as ≥ 2% drop in weight from the time of admission to discharge. Patients were divided into two groups, those showing a ≥ 2% drop in weight from admission to discharge and those that showed either an increase in weight or < 2%/no change from admission to discharge.

Diagnostic utility of serum pre-albumin in predicting weight loss was calculated using a two-by-two contingency table with weight loss as gold standard. Sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of serum pre-albumin against weight loss were also computed.

We used an ROC curve to determine the best serum pre-albumin cut-off point for predicting weight loss in hospitalised children. The area under the ROC curve (AUROC) was used to determine extent to which serum pre-albumin predicted weight loss. Discriminative power of the AUROC was categorised as: (i) not discriminative (< 0.5), (ii) poor–fair discrimination (0.5–0.7), (iii) acceptable discrimination (0.7–0.8), (iv) excellent discrimination (0.8–0.9) and (v) outstanding discrimination (≥ 0.9).

Risk of malnutrition on admission using levels of serum pre-albumin was summarised using a pre-albumin risk stratification model by Bernstein *et al.*[17] where normal = 0.15–0.35 g/l, increased risk of malnutrition = 0.11–0.14 g/l, significant risk of malnutrition = 0.05–0.10 g/l and poor prognosis = < 0.05 g/l.

Results

A total of 210 patients were assessed for eligibility with 170 participants fulfilling the inclusion criteria (Figure 1).

The median age of participants was 39.5 months (IQR 15–89 months). The majority (62.4%) of the patients were below the age of 60 months. Ninety participants (52.9%) were boys and 80

Table 1: General characteristics of patients admitted to the hospital children's ward

Variable, *n* = 170	Frequency (%)
Sex (%)	
Male	90 (52.9)
Female	80 (47.1)
Age (months)	
1 to ≤ 12	29 (17.1)
> 12 to ≤ 24	32 (18.8)
> 24 to ≤ 60	45 (26.5)
> 60 to ≤ 144	47 (27.6)
>144	17 (10.0)
Diagnosis on admission	
Gastrointestinal conditions	65 (38.2)
Respiratory conditions	48 (28.2)
Neurological conditions	27 (15.9)
Others (haemato-oncological, endocrinological, cardiac, surgical, nephrological)	30(17.7)
Duration of hospital stay (days)	
2 to ≤ 3	66 (38.8)
> 3 to ≤ 5	72 (42.4)
> 5 to ≤ 7	17 (10.0)
> 7	15 (8.8)

Note: AKUH,N = Aga Khan University Hospital, Nairobi.

(47.1%) were girls, and the duration of hospital stay ranged from 2 to 25 days (median three days; IQR 2–4). Gastrointestinal system conditions (mainly acute gastroenteritis and gastritis) were the most common on admission followed by respiratory system and central nervous system conditions (Table 1).

The median weight on admission was 14.8 kg (IQR 10.2–23.4). At discharge the median weight dropped to 14.15 kg (IQR 9.88–23.3) and a mean drop of 0.5 kg (SD ± 3.37) was observed.

All age groups demonstrated a reduction in weight during hospitalisation; however, it was more common in children aged 12–24 months (23/32, 71.9%), and lowest in those aged < 12 months (14/29, 48.3%). The greatest weight lost was observed among children diagnosed with gastroenteritis (26/32, 81.3%), gastritis (9/14, 64.3%) and pneumonia (10/18, 55.6%).

Ninety-seven (57.1%) patients showed a decrease in their serum pre-albumin levels within 48–96 h post admission. Of the 103 (60.6%) patients who lost weight from admission to discharge, 70 (68%) demonstrated a decrease in serum pre-albumin ($p < 0.001$).

Table 2: Diagnostic utility of serum pre-albumin using anthropometry as gold standard

Test		Weight loss ≥ 2%		Total
		Positive	Negative	
Serum pre-albumin < 0.15 g/l	Positive	79	44	123
	Negative	24	23	47
	Total	103	67	170

The sensitivity and specificity of serum pre-albumin using a cut off level of < 0.15 g/l on admission in predicting weight loss were 76.7% (CI 67.3–84.5%) and 29.0% (CI 18.2–42.0%) respectively, with a negative predictive value (NPV) of 42.9% (CI 30.8–55.9%) and a positive predictive value (PPV) of 64.2% (CI 59.7–68.5%). Similarly, the positive likelihood ratio (LR+) and negative likelihood ratio (LR–) were 1.08 and 0.8 respectively (Table 2).

A graph of sensitivity versus specificity for serum pre-albumin in predicting children at risk of weight loss demonstrated a cross-over point for sensitivity and specificity curves at 55%, which corresponded to serum pre-albumin level of 0.11 g/l (Figure 2). The best cut-off point for serum pre-albumin in predicting weight loss in hospitalised patients was thus identified to be 0.11 g/l. Using this value, sensitivity dropped to 64.1% (95% CI 56.9–71.3) with an increase in specificity to 49.3% (95% CI 41.7–56.8).

The majority of the patients (72.3%) on admission were already at risk of malnutrition as determined by the pre-albumin risk stratification model of Bernstein *et al.*[17] (Table 3). Nutritional status deteriorated in 19.4% (33/170) from admission to discharge based on this model (Fisher's exact test < 0.001). Only 1.8% (3/170) of patients had an increase of ≥ 2 mg/dl (0.02 g/l) per day, the cut-off point indicating adequate nutritional support in hospitalised patients.

Discussion

Currently, there is no consensus on the ideal method of assessing acute malnutrition occurring within the hospital setting. Although anthropometry is most commonly used as the reference, it is inappropriate for detecting acute nutritional changes over the period of a short hospital stay. Serum pre-albumin has hence been proposed as a surrogate marker for detection of early protein malnutrition in situations of short hospital stay.[9,11]

As a measure of nutritional status, our study found 57.1% of patients had a drop in their serum pre-albumin levels within 48–96 h post-admission. This incidence compared well with anthropometric assessment where we found 60.6% of children to have lost weight over the same period, a mean loss of 0.5 kg that corresponded to a 0.17% daily weight loss, which is the critical threshold for an adverse clinical outcome reported by Meritt and Blackburn.[18]

Of those 103 patients who demonstrated a drop in weight from admission to discharge, 70 (68%) had a drop in serum pre-albumin ($p < 0.001$). To our knowledge, there is only one other study[15] in children comparing serum pre-albumin and anthropometric measurements. However, unlike our study, that study was in an outpatient setting. The authors demonstrated that serum pre-albumin was not only able to distinguish between various grades of malnutrition, but was also the only parameter which could differentiate mild protein energy malnutrition (PEM) from normal when anthropometry, including weight, height and mid-arm circumference, was not sensitive to do so.

In our study, serum pre-albumin had a fairly good sensitivity (76.7%) but a poor specificity (29.0%) with low positive and negative predictive values. The ideal biochemical marker would be one that has a high sensitivity and specificity and also high positive and negative predictive values. These results are similar to those by Bulent *et al.*[16] who demonstrated serum pre-albumin's sensitivity, specificity, positive and negative predictive values in

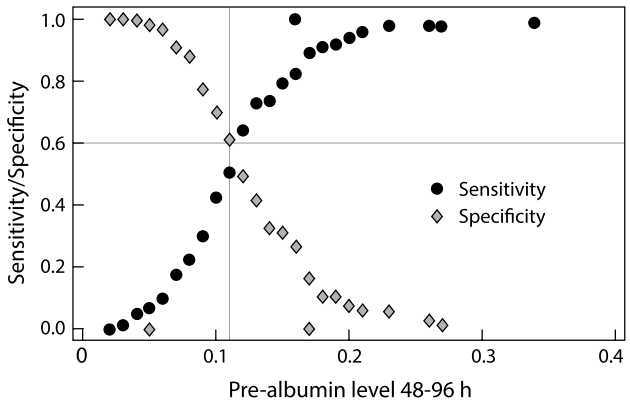

Figure 2: Comparison of sensitivity and specificity of serum pre-albumin to determine best cut-off point.

Table 3: Comparison of nutritional risk at time of admission and discharge using Bernstein's pre-albumin risk stratification model

Pre-albumin risk stratification	Admission, no. (%)	48 hrs post-admission, no. (%)
Normal (0.15–0.35 g/l)	47 (27.7)	42 (24.7)
Increased risk for malnutrition (0.11–0.14 g/l)	55 (32.3)	50 (29.4)
Significant risk for malnutrition (0.05–0.10 g/l)	63 (37.1)	70 (41.2)
Poor prognosis (< 0.05 g/l)	5 (2.9)	8 (4.7)
	170 (100.0)	170 (100.0)

Source: Bernstein *et al.*[17]

the assessment of risk of malnutrition in an adult population as 94%, 32%, 67% and 78% respectively. The low specificity can be explained by the fact that serum pre-albumin levels are affected by a number of other factors including zinc deficiency, use of steroids, severe renal and liver disease, and malignancy.

Although the positive and negative likelihood ratios were low, these ratios offer extra benefit to clinicians as they are independent of disease prevalence and can be used to quantify the probability of disease in an individual patient. According to our study, the best cut-off point for serum pre-albumin in predicting weight loss in hospitalised patients was 0.11 g/l. Using this value, sensitivity dropped marginally; however, an increase in specificity was observed.

The majority of patients were already at risk of malnutrition at the time of admission based on the pre-albumin risk stratification model of Berstein *et al.*[17] Our study showed that 19.4% of children had worsening of their nutritional status based on this model. In this respect, serum pre-albumin concentration on admission is useful in identifying at-risk patients who require careful monitoring and nutritional support while in hospital.

In this study only 1.8% of patients had a rise in serum pre-albumin of 2 mg/dl per day, the cut-off to suggest adequate nutritional support.[9] Therefore, apart from assessing overall nutritional status in hospitalised patients, low serum pre-albumin may be used to identify patients requiring nutritional support to prevent malnutrition during hospital stay and may have some utility in predicting outcomes like duration of hospital stay when admission pre-albumin levels are low.

Conclusions

Malnutrition is an important problem among hospitalised patients affecting children of all age groups and is often overlooked during inpatient care. Currently there are limited data on the use of serum pre-albumin as a nutritional screening tool, but this study has highlighted the diagnostic utility of its use in predicting weight loss among hospitalised children. Although it may have some use in identifying and monitoring nutritional status, it is only moderately sensitive in predicting weight loss among hospitalised children.

Further studies on the utility of various screening tools for identifying and monitoring patients at risk of hospital malnutrition on admission and during hospitalisation are needed.

Study limitations

A precision error of 7.5% was used for estimation of sample size estimation, due to time restrictions. However, estimation of 95% CI provides the level of precision attained. A larger study would have provided more power to attain a closer interval.

Roles of authors

Del-Rossi Sean Quadros – Principal Investigator. Conceptualisation, design and execution of the study, preparation of the manuscript.

Rose Kamenwa – Secondary Investigator. Conceptualisation, design, content expert, review and editing of manuscript.

Samuel Akech – Secondary Investigator. Methodology and data analysis, review and editing of manuscript.

William Macharia – Secondary Investigator. Conceptualisation, design, methodology and analysis, review and editing of manuscript.

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