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Use of Plasma Prealbumin concentration in assessment of nutritional status of adult patients admitted in rural Hospitals in Rivers State, Nigeria

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Abstract: *Protein-energy malnutrition (PEM) is a common condition among patients admitted to hospitals, and it is associated with a worse prognosis and increased mortality. Although several screening systems are now available, PEM is still poorly recognized especially in the rural settings as there is no consensus on which test is more reliable and feasible in clinical practice. Prealbumin (PAB) is a potential useful PEM marker because its serum concentrations are closely related to early changes in nutritional status.*

We studied PEM prevalence and PAB serum concentrations in 120 hospitalized patients. The Detailed Nutritional Assessment (DNA) was used as the reference method to determine PEM. PAB performance was compared with that of 2 other methods, the Subjective Global Assessment (SGA) and the Prognostic Inflammatory and Nutritional Index score (PINI).

According to the DNA reference method, 51% of patients were classified with mild malnutrition and 23% with severe malnutrition. PAB showed the best concordance with the standard DNA method (concordance index, 80%) and a good sensitivity/specificity profile (84.9%/78.9%) compared with SGA and PINI.

We conclude that PAB could represent a feasible and reliable tool in the evaluation of nutritionalstatus, especially in rural settings where it is difficult to obtain a more detailed and comprehensive nutritional assessment such as the DNA.

Keywords: *Protein-energy Malnutrition, Prealbumin, Admitted-adult-patients, rural- hospitals, Rivers State.*

I. Introduction

Protein-energy malnutrition (PEM) is a chronic or acute lean body protein loss that leads to a state of specific nutrient deficiency that produces a measureable change in body function. PEM is associated with a worse outcome during illness and may be reversed by conversion to an anabolic state. PEM is common in hospitalized patients and is associated with increased mortality [1,2]; 30-60% of patients hospitalized for acute illness are malnourished, and nutritional status has been shown to deteriorate during hospitalization [3]. Reasons for this high prevalence include poor recognition and monitoring of nutritional status and inadequate intake of nutrients during hospitalization [4]. Malnutrition is also a major problem among residents in long-term care facilities. Furthermore, patients admitted to the hospital may already be malnourished or at risk of malnutrition. For many diseases, implementation of validated procedures for the early identification of malnourished patients is important for improving treatment response.

Anthropometric measurement (e.g. of triceps skin-fold thickness or arm-muscle circumference), an early method of nutritional assessment, has been shown to be an inaccurate indicator of nutritional status [2]. Several tools to assess malnutrition have been subsequently developed, many based on subjective evaluation from the operator, such as the Subjective Global Assessment (SGA) [5,6]. This method is based on the assessment of conditions associated with risk of malnutrition and on a physical examination that includes relevant features such as weight loss and loss of subcutaneous fat. A patient generated SGA is an alternative tool that includes data provided by the patient [7]. The Mini Nutritional assessment has been developed specifically for geriatric patients. Like the SGA, it includes evaluation of risk factors associated with malnutrition and additional information on nutritional habits [8].

The use of subjective assessment is very skill dependent and can result in underestimation of malnutrition risk. Alternative methods are based on the evaluation of individual biochemical variables, such as measurement of prealbumin (PAB) [9-11] or retinol binding protein (RBP) [12], or of multiple variables, as in the Prognostic Inflammatory and Nutritional Index (PINI) score [13], which includes evaluation of albumin,∝1-acid glycoprotein, and C-reactive peptide (CRP). Other tools, such as the Detailed Nutritional Assessment (DNA) [14], are based on the combination of both approaches and include history, physical examination, and biochemical data. An international consensus on a reference method is yet to be established. The DNA can be considered one of the most comprehensive methods, but it is time-consuming, costly, skill dependent, and unsuitable for large scale use. Therefore, there is a need for a method that is easy to use inclinical practice and

especially in rural settings with adequate specificity and sensitivity to assess nutritional status in hospitalized patients.

Prealbumin has been shown to be a useful marker in monitoring malnourished patients as its serum concentrations are closely related to early changes in the nutritional status and it changes in response to nutritional support [11, 15-17]. We tested the feasibility, sensitivity and specificity of selected screening methods, namely SGA, PINI, PAB and RBP, compared with DNA, which we used in this study as a reference method.

II. Subjects and methods

We enrolled 120 patients (50 males and 70 females) admitted to 15 rural hospitals in Rivers State from February to May, 2006. Patients age ranged from 25 to 95 years (mean, 65 years). The study included patients admitted to general hospitals and government owned cottage hospitals in the rural communities of Rivers State. In all the cases, admission was for conditions that did not require surgery. Patient's characteristics are summarized in Table 1. The study protocol was approved by the Local Government Council Review Board in the affected Local Government Areas of theState and the management of the hospitals involved.Informed consent was obtained from all participants. All nutritional assessments and biochemical testing were performed on the 4th day after admission as follows:

Detailed Nutritional Assessment (DNA) included chart review for height and weight, unintentional weight changes over the previous 3 months, total lymphocyte count, serum albumin concentration, total cholesterol concentration, body mass index, energy requirements and intake during a 24-hour period, and the presence of risk factors for malnutrition. Energy intakes were obtained by use of nutritional records of caloric intakes completed during the first 3 days of the hospital stay. The records were completed by the patientwith the assistance of caregivers. Nutritional needs were calculated with the Harris-Benedict formula corrected for activity and stress factor. Each criterion was scored as described by Azad et al [14], leading to 3 categories of patients: normal (score 7-11), mild malnutrition (score 12-15), and severe malnutrition (score >15).

Subjective GlobalAssessment (SGA) was based on the patient's history and physical examination. The clinical features addressed in the history were weight loss in the previous 6 months and the presence or absence of gastrointestinal symptoms such as anorexia, nausea, vomiting and diarrhoea. The physical examination included subjective assessment of the loss of subcutaneous fat over the triceps and midaxillary line of the lateral chest wall, muscle wasting in the deltoids and quadriceps, and the presence of ankle oedema and/or ascites. According to established criteria [5, 6] patients were classified as class A (normal), class B (mild malnutrition), or class C (severe malnutrition).

Prealbumin (PAB) and Retinol Binding Protein (RBP) were assessed in accordance with previously proposed criteria [15]. Patients were classified in 3 categories: normal, with PAB serum concentrations> 0.17g/L; mild malnutrition, with concentrations of 0.10-0.17g/L; and severe malnutrition, with concentrations<0.10g/L. The RBP, cutoff values were as follows: normal, with RBP concentrations > 0.03g/L; mild malnutrition, with concentrations of 0.02-0.03g/L; and severe malnutrition, with concentrations < 0.02g/L (modified from Ingenbleek et al [12].

For Prognostic Inflammatory and Nutritional Index (PINI) scoring, we based on the measurement of the plasma concentrations of albumin, ∝1-acid glycoprotein, and C - reactive protein (CRP). We reduced the original 5-category classification [13] to 3 categories: normal (PINI score < 1), mild malnutrition (PINI score 1-20), and severe malnutrition (those originally classified as "risk for death"; PINI score > 20).

Laboratory measurements of PAB, RBP, and albumin were by nephelometric assay (BNII, Laser Nephelometer, Dade Behring). Total cholesterol was measured by the automated cholesterol oxidase: P-aminophenazone (CHOD-PAP) method, CRP and ∝1-acid glycoprotein by turbidimetric methods (Modular PP, Roche), and lymphocyte counts by ADVIA 120 (Bayer). All procedures were in accordance with quality service standards.

III. Statistical Methods

We used current criteria for the assessment of diagnostic tests, including concordance, sensitivity, and specificity, to evaluate the validity of methods used as alternatives to the DNA method, which served as the reference or gold standard. Agreement between DNA and the other nutritional assessments was also assessed with the Cohen (κ) test, designed to measure the interrater agreement. Cohen (κ) agreement was defined as "poor" ifκ was ≤ 0.20, "fair" if κ was >0.20 and≤ 0.60, "substantial" if κ as > 0.60 and ≤ 0.80, and "good" if κwas > 0.80 [18].

IV. Results

Patients characteristics are shown in Table 1 and the nutritional laboratory parameters of the 120 patients used for this study are summarized in Table 2. For each method, percentages of patients in each

category were as follows: DNA, 51% mild malnutrition and 23% severe malnutrition; SGA, 47% mild malnutrition and 18% severe malnutrition; PINI, 45% mild malnutrition and 33% severe malnutrition; PAB, 50% mild malnutrition and 20% severe malnutrition (Table 3). Given the highly significant correlation between PAB and RBP ($r = 0.79$; $P < 0.001$), and also taking into account the potential influence of chronic renal failures on RBP [12, 15], we decided to use only PAB in the nutritional evaluation.

Prealbumin (PAB) showed the best concordance with the DNA reference method (concordance index, 80%). Corresponding values for SGA and PINI were 64% and 65% respectively. Cohen test κ values were 0.68 for PAB (indicating a strong agreement), 0.44 for PINI (fair agreement) and 0.41 for SGA (fair agreement).

After combining mild and severe malnutrition into a simple group, we evaluated the degree of sensitivity and specificity of different methods. Results for sensitivity/specificity with DNA as the reference methods were as follows: SGA, 75.1%/81.4%; PINI, 80.2%/63.7%; and PAB, 84.9%/78.9%. All methods showed good sensitivity. PAB showed the best sensitivity (84.9%), and SGA showed the best specificity (81.4%). PINI showed intermediate results, with good sensitivity and relatively poor specificity.

We found that only 21% of patients achieved at least 80% of their calculated nutritional need. However, we found no significant difference between DNA and PAB for patients reaching versus not reaching 80% of their required energy intake.Similarly, after stratification of malnourished and normally nourished patients, we observed no differences in mean PAB values when we compared patients above and below their 80% energy intake.

C-reactive protein (CRP)plasma concentrations were increased in 83 patients (69%). We found a statisticallysignificant inverse correlation between PAB and CRP ($P < 0.05$). Inspiteof the inverse relationship between PAB and CRP, we observed very good concordance between PAB and DNA at high and low CRP concentrations (Table 4), with concordance indexes of 80.6% and 78.0% for high and low CRP concentrations respectively.

V. Discussion

Protein energy malnutrition is a clinical condition characterized by depletion of muscle/body fat and visceral proteins and associated with increased morbidity and mortality. Protein energy malnutrition (PEM) in hospitalized patients has been traditionally considered a relatively rare condition affecting mainly the elderly and patients with severechronic diseases, cancer or protracted nutrients losses. Several studies have shown that malnutrition affects 30% -60% ofhospitalized patients [2, 3, 19]. Hypercatabolic states associated with acute or chronic disorders are important PEM determinants. On the other hand, a decreased food intake can be due to lack of assistance during meals, deglutition disorders, food withdrawal while waiting for radiologic or endoscopic investigations, mental confusion, and feeding refusal. Failure to identify these nutritional risk factors in patients early during the hospital stay can lead to health deterioration and increased length of stay, with associated costs [19-21].

Detailed nutritional assessment (DNA) can be considered a reliable procedure to identify patients at risk of malnutrition, but this method is time-consuming and difficult to use on a large scale. In the last few years, many nutritional screening tools have been developed, tested and implemented inclinical practice, several combining laboratory tests and patient information [22]. Biochemical markers have always been an attractive option because they are easier to introduce and standardize in clinical practice. Albumin is a traditional marker of nutritional status, but its large body pool, with a half-life of 20 days, and its sensitivity to the patients hydration state make it too sensitive to be used to assess PEM. Prealbumin (PAB) is a better nutritional marker because it has a short half-life (48hours), a relatively small body pool, and a rapid rate of synthesis that responds to protein intake [9]. Plasma PAB concentration has been shown to significantly decrease only 3 days after inadequate nutrient intake [16], and to increase 1mg/day when the nutrient needs are satisfied [17]; plasma PAB can be influenced by an acute or chronic renal insufficiency [16].

Our prevalence data, which showed that 74% of patients had variable degrees of malnutrition (Table 3), are in agreement with the literature [1-3] even though our own percentage is a little higher because of the rural environment (in a developing country) of our study. The higher percentage of patients with severe malnutrition identified with PINI can be explained by the fact that this method is affected by plasma concentrations of acute-phase proteins indicative of a stress hypermetabolic response. In our study group, only 25 patients (21%) achieved at least 80% of their calculated nutritional need, a cutoff value that has been shown to correlate with a high risk of malnutrition during hospitalization [23].

Our results showed various degrees of concordance between DNA and the alternative methods investigated. Among these, PAB showed the best concordance with DNA and a good sensitivity/specificity profile. A major limitation to the use of biochemical markers is that their plasma concentrations may be influenced by pathogenic conditions. In particular, PAB concentrations decrease in the presence of inflammation (negative acute-phase reactant). The inverse correlation between PAB and CRP concentrations may represent a confounding factor in the interpretation of the results. Plasma PAB concentrations change rapidly; a decrease of

up to 50% in PAB concentration is expected after few days of inadequate nutrient intake and/or diseases with an acute phase response, conditions that often coexist in severely ill patients [24]. Conversely a rapid increase of PAB concentration is seen when adequate nutritional intake is restored [21] or CRP stabilizes [25]; therefore rapid changes in CRP can induce an overestimation of malnutrition. Although these limitations should be taken into consideration, our data suggests that PAB can still be reliable in cases involving inflammation. A good correlation between PAB and DNA was found at both high and low CRP concentrations (Table 4). Notably, CRP and other markers of acute-phase response are not included in the DNA score calculation.

VI. Conclusion

Our study results indicate that PAB is an inexpensive, feasible, and reliable tool in the evaluation of malnutrition affecting hospitalized patients, particularly in rural settings in the developing countries where it is difficult to perform a more detailed and comprehensive nutritional assessment such as DNA. Further investigation with sequentialmeasurements is needed to elucidate the complex relationship between PAB and inflammation and clarify the role of PAB in monitoring the efficacy of nutritional interventions.

Table 1: Characteristic of the study participants

	Number	%
Age, mean (Range)	**65(25-95)**	
Sex		
Female	70	58
Males	50	42
Clinical Condition*		
Diabetes	40	33
Cerebrovascular accident (Stroke)	20	17
Cancer	18	15
Congestive heart failure	34	28
Infection	30	25
Trauma	21	18
≥ 2 conditions	58	48
Nutritional Variables		
> 5% unintentional weight loss over 3 months	41	34
≥ 80% energy need intake	25	21
Laboratory Values		
Albumin < 2.8g/L	40	33
Cholesterol < 4.7mmol/L	48	40
Lymphocyte count < 1200/fl	38	32
C-reactive protein> 5mg/L	83	69

Note:

* Patients may be affected by more than one disease.

Table 2: Patients Laboratory and Nutritional values

	Range	Mean (SD)
Body mass index, kg/m^2	11.0-42.2	23.7 (4.7)
Albumin, g/L	1.3-4.9	3.3(0.8)
Prealbumin, g/L	0.01-0.35	0.14 (0.04)
C - reactive protein, mg/L	0.2-250.0	37.5 (45.0)
RBP, g/L	0.01-0.09	0.04 (0.02)
∝1-Acid glycoprotein, g/L	0.17-2.72	1.33 (0.45)
24-hourcaloric needs, kcal	1000-3000	1630 (330)
24-hour caloric intakes, kcal	239-2350	1095 (398)
Difference (decrease) of intake Vs needs, %	17-180	70.9 (24.6)

Note:

RBP: Retinol Binding Protein

Table 3:Prevalence of malnutrition assessed using different methods in 120 patients

	Normal%	Mild malnutrition%	Severe malnutrition %
DNA (reference method for this study)	26	51	23
SGA	35	47	18
PINI	22	45	33
PAB	29	50	21
RBP	26	54	20

Note:

DNA: Detailed Nutritional Assessment

SGA: Subjective Global Assessment

PINI: Prognostic Inflammatory and Nutritional Index score

PAB: Pre-albumin

RBP: Retinol Binding Protein

Table 4: Prevalence of Malnutrition in 120 patients assessed by PAB and DNA at different concentrations of C - reactive protein (CRP)

	Total (120 patients)	PAB ≥ 0.17g/L (Normal)	PAB < 0.17g/L (Malnutrition)*	DNA score ≤ 12 (Normal)	DNA score > 12 (Malnutrition)*	Concordance index PAB/DNA, %
CRP > 5mg/L, n(%)	83 (69)	21 (25)	62 (75)	23 (28)	60 (72)	80.6
CRP ≤ 5mg/L, n (%)	37 (31)	29 (78)	8 (22)	26 (70)	11 (30)	78.0

* Mild + severe malnutrition

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