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THE RELATIVE ROLE OF SERUM ALBUMIN AND URINARY CREATININE AS BIOCHEMICAL INDICES FOR NIGERIANS WITH PULMONARY TUBERCULOSIS.

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Objective: The objective is to evaluate roles of urinary creatinine and serum albumin as biochemical markers for monitoring the nutritional status of pulmonary tuerculosis patients during treatment. **Design**: This was a longitudinal study. Each patient was studied for six months. **Settings**: This study was carried out at University of Ilorin Teaching Hospital. **Subjects**: Forty-five newly diagnosed patients with pulmonary tuberculosis were used for the study. **Intervention (Method):** Forty-five newly diagnosed pulmonary tuberculosis patients were placed on six months short course regimen. Their weight, Body mass index, serum albumin and 24-hour urinary creatinine were determined before treatment, at the end of the 1st, 2nd, 4th and 6th month of treatment. Using ANOVA, the mean values of the weight, BIM and serum albumin were analysed with further analysis paired student T- test of the pre-treatment values with end of 6th month values. **Main outcome measured**: Their weight, body mass index, serum Albumin and 24-hour urinary creatinine were determined. **Results**: Thirty-one patients with mean age of 36.8 years completed the study. The pretreatment mean weight, body mass index, serum albumin were 49.53kg, 17.72kg/m^2 and 26.7g/L respectively. The corresponding values at the end of the sixth month of treatment were 57.03kg. 20.4kgm^2 and 39.97g/L. These three variables showed significant upward improvements. **Conclusion**: Both the body mass index and serum Albumin pretreatment values showed that the patients were malnourished at presentation. Serum albumin being more sensitive and more reliable than both weight and body mass index as revealed by this recommended as index for nutritional assessment in patient with tuberculosis.

INTRODUCTION

There is an established association between pulmomary tuberculosis and malnutrtion. Morbidtiy is over three times greater for underweight patients than for overweight ones. Health education on nutrition is therefore an integral part of the management of patients with pulmonary tuberculosis.[1]

Compliance with this nutritional advice is usually monitored by weighing the patient during their clinic visits.

Weighing machines need frequent re-calibration if the result obtained will be reliable. Bouts of diarrhoea or vomiting after taking the oral drugs will reduce the reliability of the weight in assessing the nutritional status of the patients. The value of plasma prealbumin as a biochemical parameter for monitoring nutrition in pulmonary tuberculosis has been established[2]. However the high cost and the non- availability of the assay in most medical centres in the developing countries where pulmonary tuberculosis is prevalent put a serious limitation on the use of plasma prealbumin as an alternative to simple weighing.

Albumin has a half- life of 21 days. It is a good index of body nutrition, more so for patients with pulmonary tuberculosis that have an average of monthly visits to their clinics. Creatinine is produce from creatine and phoshate in skeletal muscle, and is excreted in the urine. Urine creatinine excretion depends on muscle mass and it has been estimated that 1g (9mmol) of creatinine is derived from 17kg of skeletal muscle.[3] Twenty–four hour urinary creatinine excretion correlated well with total body muscle mass.[4]

Urinary excretion of creatinine is a recongnized biochemical index for laboratory assessment of nutrition.[5]

This study therefore was carried out to determine the degree of malnutrition amongst patients with pulmonary tuberculosis using their body mass index and to evaluate the value of urinary creatinine and serum albumin as biochemical markers for monitoring the nutritional status of pulmonary tuberculosis parients during treatment.

MATERIALS AND METHOD.

All patients were newly diagnosed pulmonary tuberculosis patients from the chest clinic of the University of Ilorin Teaching Hospital. Patients that were included in the study were sputum positive on direct smear by Zhiel Nelson stain: a supportive chest x-ray finding was also mandatory. Those with human immunodeficiency virus infection, evidence of carcinoma or any protein loosing disease were excluded. These patients had six months, short course anti-tuberculous drug regimen. This consists of Isoniazid, Rifampicin, Ethambutol and Pyrazinamide. Pyrazinamide and Ethambutol were used only for the first two months of the therapy.

Each individual was weighed wearing light clothing only and without shoes, on a UNICEF Beam Balance scale. Height was measured using the vertical attachment to the scale keeping the head so that the line from the external auditory meatus to the lateral angle of the eye was horizontal. Quetelet's index was calculated from height and body weight measurements. 24-hours urine collection was done to determine 24-hours creatinine excretion. Blood (10ml) was drawn from one of the antecubital veins, with minimum stasis. Serum was separated by centrifugation after the sample had fully retracted. Where analysis was not possible on a same-day basis, the serum was preserved deep-frozen at -20^{0}c till the following day.

This study was a longitudinal one. Each patient was followed up for a period of six months that the treatment lasted. All indices, urine and blood samples were taken on the first day of visit before commencement of therapy. Subsequent samples were collected from the patients at the end of the 1st, 2nd, 4th, and 6th, months of therapy. Drug compliance and effectiveness of therapy was assesed by a combination of pill counting, urine colour changes with rifampicin, and examination of sputum for acid fast bacilli on each visit.

Serum Albumin was estimated by the bromocresol dye-binding technique.[6] Creatinine was determined using Rebery Folin method based on jaffe's reaction.[6]

Statistical analyses were carried out in an IBM-compatible personal computer using SPSS software. A one-way ANOVA was done for mean values of body weight, body mass index (BMI), serum albumin and 24-hour urinary creatinine excretion: with further evaluation using the paired student t-test. Association between body weight and BMI on one hand and biochemical indices of serum albumin and 24-hour urinary creatinine excretion was evaluated by analysis of the corresponding paired T-Test results.

RESULTS

45 patients started the study, 14 of them were lost to follow up; while only

31 completed the study. The 31 patients were made up of 17 males and 14 females with a mean age of 36.8 years. These patients by using their pretreatment data served as their own controls against which their subsequent data were compared.

Table I shows the mean values of their weight, body mass index (BMI), albumin (ALB) and 24-hour urinary creatinine excretion (UCRE). The mean weight before treatment, end of 1st month, end of 2nd month, end of 4th month and at the end of 6th month was 49.53kg, 51.32kg, 52.81kg, 55.27kg and 57.03kg respectively. The corresponding values for BMI was 17.72kg/m^2, 18.37kg/m^2, 18.91kg/m^2, 19.79kg/m^2 and 20.46kg/m^2. The mean serum albumin levels before treatment; end of 2nd month, end of 4th month and end of 6th month was 26.71g/L, 31.00 g/L, 34.61 g/L, 37.45 g/L, and 39.97 g/L, respectively. The corresponding values for 24-hour urinary creatinine excretion was 9322mmol, 8910mmol, 8914mmol and 9397mmol. Both the BMI and serum albumin pretreatment values show clearly that these patients were malnourished at presentation.

A one-way analysis of variance was used to compare the various means obtained for each variable.

Table II shows that the F-probability for weight. BMI, Albumin and 24-hour urinary creatinine excretion was 0.031, 0.002, 0.001 and 0.904 respectively. These show that with the exception of the 24-hour urinary creatinine excretion the other three variables of weight, BMI and serum albumin had statistically significant changes amongst their mean values.

Table III shows the result of further analysis with paired sample T-test, using the pretreatment and post treatment (end of 6th month) value. The critical ratio calculated (t-value) was – 7.450, - 7.333, - 11.691 and 0.15 for weight, BMI, albumin and urinary creatinine respectively, while their corresponding P – values were 0.0001, 0.0001, 0.0001 and 0.882 respectively. The correlation coefficient for each pair was 0.846, 0.763, 0.756 and 0.432 respectively. This shows that there were significant differences in the mean pretreatment values of weight, BMI and albumin when compared with their end of treatment mean values.

TABLE 1

MEAN VALUES OF WT, BMI, ALB and UCRE

	Pretreatment	End of 1st Month	End of 2nd Month	End of 4th Month	End of 6th Month
WEIGHT (WT) kg	49.53	51.32	52.81	55.27	57.03
BODY MASS INDEX (BMI) kg/m^2	17.72	18.37	18.91	19.79	20.46
ALBUMIN (ALB) g/L	26.71	31.00	34.61	37.45	39.97
24 HOUR URINARY CREATININE EXCRETION mmol/24hrs (UCRE)	9322	8910	8752	8914	9397

TABLE II

ANOVA RESULTS OF WT, BMI, ALB, AND UCRE

Sources of variation	Degree of freedom	Sum of square	Mean square	Variance Ratio	F. Probability
WEIGHT					
Time	4	1119.7	279.9	2.74	0.031
Residual	150	15352.0	102.3		
Total	154	16471.7			
BODY MASS INDEX					
Time	4	149.273	37.318	4.42	0.002
Residual	150	1265.792	8.439		
Total	154	1415.065			
ALBUMIN					
Time	4	3411.20	852.80	10.29	,0.001
Residual	150	12432.39	82.88		
Total	154	15843.59			
URINARY CREATININE EXCRETION					
Time	4	9.935E+06	2.484E+06	0.26	0.904
Residual	150	1.437E+09	9.580E+06		
Total	154	1.447E+09			

TABLE III

PAIRED T-TEST OF PRETREATMENT AND END OF 6TH MONTH (POST-TREAT) WT, BMI, ALB, AND UCRE VALUES

	t	df	Sig. (2-tailed)	Correlation
Weight	-7.450	30	<0.0001	.846
Body mass index	-7.333	30	<0.0001	.763
Albumin	-11.691	30	<0.0001	.756
24 Hour Urinary Creatinine	0.15	30	0.882	.432

DISCUSSION

A clear association between BMI and incidence of tuberculosis has been established (1,7,8). Tverdal in his work also observed that mortality from tuberculosis showed a decreasing tendency with increasing BMI. This study with a mean BMI of 17.72kg/m2 for the patients at presentation confirms the high prevalence of undernutrition amongst patients with pulmonary tuberculsis. Table one shows a steady improvement in the weight, BMI and serum albumin values of the patients as the treatment progresses. The consistent upward trend of these makers of nutritional status shows that they may be reliable parameters for monitoring tuberculosis.

Subjecting the mean values of the patient's weight, BMI, Serum Albumin and 24-hour urinary creatinine excretion to ANOVA give an F-probability of 0.031, 0.002, 0.001 and 0.904 respectively. These values show that there existed statistically significant differences in the mean values of these patients' weight, BMI and albumin as treatment progresses. This is in agreement with the earlier deduction from the simple observation of the trend in these variables.

A closer look at the calculated critical variance Ratio of 2.74 for weight, 4.42 for BMI and 10.29 for serum albumin shows that serum albumin is the most sensitive of the three variables thereby giving it an edge over both the weight and BMI as indices for assessing nutritional improvement in patients with pulmonary tuberculosis. The above observations and deductions do not hold for 24-hour urinary creatinine excretion as it fails to change significantly (P-value = 0.904). This observation could be due to a number of reasons: First, the changes in renal dynamics as a result of the drug induced hyperuricaemia associated with anti-tuberculosis drug medication. It could also be as a result of the difficulty associated with the collection of 24-hour urine samples.

Further evaluation with paired samples T-test statistical analysis involving the pre-treatment value and the post treatment (end of 6th month) values gave t-values of 7.450, 7.333, 11.691 and 0.15 for weight, BMI, serum albumin and 24-hour urinary creatinine respectively. These values further confirms that the weight, BMI and serum albumin had changed significantly, the serum albumin with t-value of 11.691 is the most sensitive while the 24-hour urinary creatinine excretion t-value of 0.15 which is below the 95 percentile value of 2.042 at 30 degree of freedom on a t-distribution table is statistically not significant.

We therefore conclude that weight, BMI and serum albumin are very reliable markers of nutritional status in patients with pulmonary tuberculosis. Of these three variables serum albumin is the most sensitive. Since serum albumin is free from some of the shortcomings of weight an BMI like the influence of drug induced vomiting and or diarrhea on weight and BMI, we are recommending this relatively easily available Biochemical marker as a replacement for simpe

weighing and calculated BMI in monitoring the nutritional status of patients with pulmonary tuberculosis.

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