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CORRELATION BETWEEN TRICEPS SKINFOLD THICKNESS AND PHASE ANGLE MEASUREMENT BY BIO IMPEDANCE ANALYSIS AS A MORTALITY PREDICTOR IN PATIENTS WITH CHRONIC KIDNEY DISEASE ON REGULAR HEMODIALYSIS

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ABSTRACT

Chronic kidney disease (CKD) incidence and prevalence rapidly increase in the whole world and usually results in bad outcomes. In Indonesia, from some nephrology departments, CKD incidence predicted around 100-150 in each million people and prevalence rate reach 200-250 cases in each million people. Patients with CKD who were not treated properly can develop to end stage renal disease (ESRD). ESRD patients on hemodialysis still have high morbidity and mortality rate around 15-20% each year. Malnutrition that found and treated at early hemodialysis is important to get the best outcome and also better quality of life for patients. Some procedures can be used to measure nutritional state. These procedures are anthropometry (body weight, arm circumference (AC), and triceps skinfold thickness (TST) measurements), laboratory (serum albumin, transferrin), DEXA, and bioelectrical impedance analysis (BIA). This cross sectional study on 52 patients aged ≥ 18 years old on regular hemodialysis twice a week for more than 3 months, in hemodialysis unit at H. Adam Malik General Hospital, Medan, Indonesia started from December 2013 until total sample collected. Correlation between each variable analyzed with Spearman correlation and linear regression. This study showed average TST measurement value in this study was 21.4 mm (7.26), phase angle (PhA) average value in this study in regular hemodialysis patients was 5.160 ± 1.29 , and correlation between TST and PhA showed moderate relation in this study with correlation coefficient value (r) 0.577.

KEYWORDS : Chronic kidney disease, triceps skinfold thickness, bioelectrical impedance analysis

INTRODUCTION

Chronic kidney disease (CKD) incidence and prevalence rapidly increase in the whole world and related with poor outcomes. Centers for Disease Control (CDC) reported that around 1999 to 2014 there are 16.8% world populations more than 20 years old have CKD. This percentage increases compared with 6 years ago, which is 14.5%. In developing countries, this incidence predicted around 40 to 60 cases in each million peoples per year. In Indonesia, from some nephrology departments, CKD incidence predicted around 100-150 in each million peoples and prevalence rate reach 200-250 cases in each million peoples.[1]

Patients with CKD who were not treated properly can be developed to end stage renal disease (ESRD). This state of kidney disease needs permanent kidney replacement treatment which could be dialysis or kidney transplantation. ESRD patients on hemodialysis still have high morbidity and mortality rate around 15-20% each year. Known factors for this fact are malnutrition and lowered muscle mass.[2]

Factors such as uremic state which cause low intake of calories and proteins, chronic inflammation, and acute and chronic comorbidities cause malnutrition which usually happens in patients with CKD on regular hemodialysis (HD). Some research found that 20-80% patients with HD have malnutrition [3,4]. Malnutrition that found and treated at early hemodialysis is important to get the best outcome and also better quality of life for patients [5]. Some procedures can be used to measure nutritional state. These procedures are anthropometry (body weight, arm circumference (AC), and triceps skinfold thickness measurements), laboratory (serum albumin, transferrin), DEXA, and bioelectrical impedance analysis (BIA). Anthropometry measurements can be done in hemodialysis centers because it was simple, practical, cheap and easy method. Validity of this anthropometry measurements can be used clinically to assess patient's nutritional state. Anthropometry is also useful for measuring body fat, lean mass, height, weight, skinfold thickness, arm circumference , and arm muscle area (AMA).[6] Skinfold thickness measurement can be used to measure body fat. It is practical and can be done with a simple training. Body fat measurement with skinfold thickness usually used in sports to monitor body fat percentage in daily practice and on competitions or in some gym area to monitor the result of loss weight training program[6]. Skinfold thickness measured with skinfold caliper on subcutaneous areas around extremities and body area because 50% of body fat lies in subcutaneous area.[7]

Bioelectrical impedance analysis (BIA) had been acknowledged for more than 20 years to measure human body compositions and nutritional state. This BIA first detected changes in cell membrane and water imbalance. BIA is a simple noninvasive tool which can repeatedly use and is not an operator dependent which lowers the possibility of human error. Thus, having a more accurate result in measuring CKD on HD patients' nutritional state[8]. Phase angle is one of parameters that can be evaluated in BIA and it describes water distribution and cell membrane integrity from human body. Phase angle is a sensitive malnutrition indicator as it describes intracellular and extracellular water distribution.[9] Phase angle can also be used as a prognostic of some conditions where cell integrity and water balance disturbed such as HIV infection, cancer, cirrhosis, pregnant woman, sepsis, and hemodialysis [5,8,10].

Methods

Patient Selection

This study was an analytic cross sectional study on 52 patients aged ≥ 18 years old on regular hemodialysis twice a week for more than 3 months, in hemodialysis unit at H. Adam Malik General Hospital, Medan, Indonesia started from Desember 2013 until total sample collected. Patients who did not agree to be included in this study and patients with irregular hemodialysis or arteriovenous fistula on both hands were all excluded from this study.

Procedure

All subjects in this study had to write and sign their written consent to be included in this study. After a written consent signed by patients, we recorded name, age, gender, weight, height, duration on hemodialysis, CKD etiologies, and BMI. Skinfold thickness for each patient measure on the right side of patient body with skinfold caliper. Subcutaneous area were pinched with first and second

finger on examiner left hand and skinfold caliper placed 1 cm distal and straight from pinched skin. Measurement recorded after 2-3 seconds and repeated 3 times with 1 mm difference from each measurement. Same patient also had their BIA recorded to get their phase angle and other parameters for their nutritional status.

Data analysis

Univariate analysis were used to get average distribution description and standard deviation value for each variable. Correlation between each variable analyzed with Spearman correlation and linear regression using SPSS 20.0 version with p value <0.05 was considered statistically significant.

RESULT

There were 52 patients with ESRD on regular hemodialysis included in this study. Characteristics population in this study described as seen in table 1 below.

Characteristics	n = 52
Age, year, mean (SD)	46.12 (10.62)
Gender, n (%)	
Male	37 (71.2)
Female	15 (28.8)
Height, cm, mean (SD)	163.6 (6.38)
Weight, kgs, mean (SD)	57.69 (10.39)
Body Mass index, n (%)	
Underweight	10 (19.2)
Normal weight	35 (67.3)
Overweight	6 (11.5)
Obese	1 (1.9)
Lab results	
Hb, mg/dl, mean (SD)	8.93 (1.26)
Ureum, mg/dl, mean (SD)	136.21 (38.07)
Creatinin, mg/dl, mean (SD)	13.43 (4.23)
BIA	
RMR, kcal, mean (SD)	1396.88 (171.45)
FFM, mean (SD)	47.22 (7.47)
% FFM, mean (SD)	81.64 (6.47)
FM, mean (SD)	10.87 (5.12)
% FM, mean(SD)	18.36 (6.47)
BCM, mean (SD)	24.53 (4.46)
Protein, kgs, mean (SD)	9.21 (2.25)
Mineral, kgs, mean (SD)	3.38 (0.69)
Glycogen, mean (SD)	431.33 (66.04)
PhA, degree, mean (SD)	5.16 (1.29)
Etiology, n (%)	
Non DM	40 (76.9)
DM	12 (23.1)
Duration on HD, n (%)	
≤ 52 weeks	19 (36.5)
> 52 weeks	33 (63.5)
TST, mm, mean (SD)	21.24 (7.26)
PhA, degree, mean (SD)	5.16 (1.29)

RMR :Resting Metabolic Rate, FFM :Free Fat Mass,FM :Fat Mass, BCM :Body Cell Mass

Nutritional status description for all subjects devided by their etiology that caused ESRD (diabetic and non-diabetic). Table 2 showed that there were significance statistical differences in some variables (creatinine, protein and PhA value) with p value <0.05 and no significance statistical differences in other variables with p value <0.05.

Table 2. IMT, Hemoglobin, Ureum, Creatinine, TST, and BIA Parameters Differences According to Etiology of CKD

Variable	Non DM (n=40)	DM (n=12)	P value
BMI, kg/cm^2 mean (SD)	21.56 (3.34)	21.16 (2.38)	0.700[a]
Laboratorium			
Hb, mg/dl, mean (SD)	8.85 (1.26)	9.17 (1.28)	0.455[a]
Ureum, mg/dl, mean (SD)	138.76 (37.90)	127.73 (39.03)	0.384[a]
Kreatinin, mg/dl, mean (SD)	14.22 (4.12)	10.77 (3.56)	0.012[a]
TST, mm, mean (SD)	21.93 (7.53)	19 (6.03)	0.326[b]
BIA			
RMR, kcal, mean (SD)	1421.63(174.75)	1314.41 (135.54)	0.057[a]
FFM, mean (SD)	47.99 (7.62)	44.63 (6.62)	0.174[a]
% FFM, mean (SD)	81.66 (6.70)	81.59 (5.87)	0.728[b]
FM, mean (SD)	11.04 (5.49)	10.31 (3.75)	0.914[b]
% FM, mean (SD)	18.34 (6.70)	18.41 (5.87)	0.728[b]
BCM, mean (SD)	25.18 (4.53)	22.39 (3.57)	0.057[a]
Protein, kgs, mean (SD)	9.63 (2.17)	7.83 (2.04)	0.014[a]
Mineral, kgs, mean (SD)	3.47 (0.67)	3.07 (0.67)	0.073[a]
Glikogen, mean (SD)	438.58 (66.74)	407.17 (60.04)	0.150[a]
PhA, degree, mean (SD)	5.38 (1.28)	4.39 (1.03)	0.018[a]

[a] *T test independent,* [b] *Mann Whitney* ;RMR :Resting Metabolic Rate, FFM :Free Fat Mass,FM :Fat Mass, BCM :Body Cell Mass

Table 3. Correlation Analysis and Linear Regression Analysis between TST and PhA

	r	R^2	linear equation	P value
TST	0.577	0.333	2.98+0.102x(TST)	0.0001

From statistical analysis with linear regression in table above, could be concluded that correlation between TST and PhA showed moderate relation with correlation coefficient value ® 0.577. This positive value means that the higher TST value the higher PhA value. Coefficient determination value (R square value) was 0.333 which meaned 33.3% of the variation in PhA value can be explained by other factors.

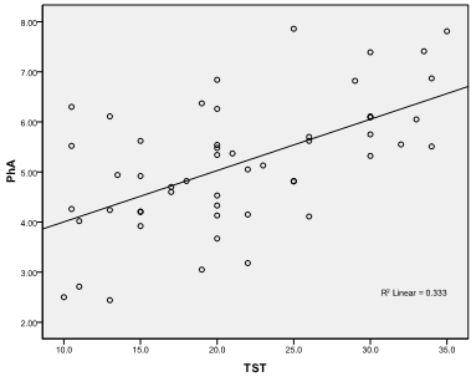

Figure 1. Scatterplot graphic of the correlation between TST and PhA

Positive predictive value (PPV) showed sickness probability in patients with positive test result. Whereas *negative predictive value* (NPV) showed patients probability without illness in negative test result. Table 4 showed PPV and NPV from TST to PhA. In this study, PhA value ≤ 5° predicted to have high mortality rate while PhA value ≥5° predicted to have low mortality rate.

Table 4. Cross Tabulation between TST and Phase Angel

		PhA	
		<5	≥5
TST	< 11	8	2
	≥ 11	16	26

Sensitivity : 8/24 = 33.3%
Specificity : 26/28 = 92.86%
PPV : 8/10 = 80%
NPV : 26/42 = 61.9%

DISCUSSION

Triceps skinfold thickness measurement in patient on regular hemodialysis used to describe correlation with other parameters for nutritional status (biochemical testing or BIA). PhA is one of the most important component in BIA. This component has a strong

correlation to patients' prognosis on regular hemodialysis.

Malnutrition prevalence rate using triceps skinfold thickness in patients on regular hemodialysis in H. Adam Malik General Hospital had not yet been done before. Seven Global Assessment and body mass index measurement are two kind of test that have been done before to get malnutrition prevalence rate. In this study, malnutrition prevalence using TST was 10 subjects (19.2%) whereas malnutrition prevalence using Seven Global Assessment in the same place was 65.3% from Ivan Ramayana study and 94.8% from Claudia Maria et al study.

Average TST measurement value in this study was 21.4 mm (7.26) with no significant difference between male and female patients. This value had a different result from other study that said triceps skinfold thickness in female was thicker than male because female has more fat mass than male. This differences could be caused by the number of male and female subjects that was not evenly distributed. Some parameters showed significant differences between male and female subjects where male had higher score than female. These parameters were BMI, creatinine, BMR, FFM percentage, BCM, protein, mineral and glycogen.

For more than 20 years BIA has been known as a noninvasive and simple technique to examine patient hydration status and this method has been successfully used to determine dry weight in patient on hemodialysis. PhA average value in this study in regular hemodialysis patient was $5,16^{\circ} \pm 1.29$ with significant different value between male and female patients. This finding had almost same value with study that was done by Ramadani et all in 2012 which had $5,32^{\circ} \pm 1.33$ in mean PhA value. Study that was done in Europe on hemodialysis populations had a higher mean PhA value because of higher body height and different body composition. This differences could affect BIA value. PhA value and BCM value are higher in other ethnics than in Asian ethnic.[11,12]

Study that was done by Madore, Wuset, and Erenest showed strong relation between anthropometry and phase angle. Some other studies found a fact that triceps skinfold thickness had more accurate value than BIA in term of evaluating body fat. The reason why researcher choose BIA was because BIA had lower mistake possibility in examination and it could be used to evaluate patient hydration status.

FFM covers all body except FM which has muscle, vital organ, bones and extracellular fluid as main components. FFM known to have strong correlation with morbidity and physical appearance. Elevation of fat mass and muscle mass in ESRD patient on hemodialysis are expected to help elevation of patient nutritional status. Low fat mass and lose of fat after some times in hemodialysis relate with higher morbidity rate in ESRD patient on hemodialysis. This also can affect their quality of life even if we have already control the inflammation and have their demographic adjusted.[13]

Relation between nutritional status and PhA is not unusual because PhA has direct correlation with cell membrane in term of its quantity and function. One person with good nutritional status has more cells in his/her body therefore that person will have higher PhA value. Lowering PhA value along with older age indicate PhA as an functional and general health indicator apart from its function as nutritional status and body composition status indicators.

PhA has superior value to predict mortality risk in patient on hemodialysis compare with TST [10,14] Maggiore et al (1996) evaluated 133 patients on hemodialysis and concluded 2.6 times mortality risk prediction in patient with PhA level $\leq 4,5^{\circ}$ for man dan $\leq 4,2^{\circ}$ for woman. Correlation between TST and PhA shows moderate relation in this study with correlation coefficient value (r) 0.577. This positive value means that the higher TST value the higher PhA value.[10]

A weak point in this study was small sample size as well as an unevenly sample size between male and female patients. More studies should be completed in order to validate triceps skinfold thickness as single parameter of combination with other laboratory parameters such as albumin to evaluate diagnostic ability. Cross sectional type in this study also a weak point due to its inability to evaluate TST role as prognostic factor.

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