

## **Markers of Malnutrition among Dialysis Naïve CKD Patients in North Central Nigeria**

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### Abstract

**Introduction:** Chronic kidney disease (CKD) has a major effect on global health, it is responsible for both direct cause of global morbidity and mortality and as an important risk factor for Malnutrition and cardiovascular disease. In Nigeria, CKD accounts for 2-8% of total admissions into tertiary Hospital. **Methods:** This is a cross-sectional study aimed at determining markers of malnutrition such Subjective global assessment (SGA), Body mass index (BMI), waist circumference (WC), Hip circumference (HC), Mid-Arm Muscle Circumference (MAMC), Triceps Skin Fold Thickness (TSFT) serum albumin, serum creatinine, total protein, serum cholesterol C-reactive protein (CRP) and correlating them among CKD patients as a determinant of malnutrition among these group of patients. Individuals between the ages of 16 – 60 years, Patients with confirmed CKD were recruited for this research. Blood samples were drawn from a forearm vein where the plasma was separated from the cells by centrifugation and the plasma was analyzed for all the variables indicated. **Results:** There were more cases of patient with low BMI among CKD patients and this was also observed more among Diabetes mellitus (DM) patient with CKD and the non-DM patient. There were 9 (31%) of diabetics versus 5 (6.3%) of non-diabetics had low BMI. OR = 6.6, 95% CI = 2.00 – 22.10; P = 0.0001. There exists no liner relationship between serum albumin to SGA. The  $r^2 = 0.11$ . There were 4 (80%) of patients with CRP >7.5mg/l and serum albumin level of <28g/l. This study also showed that 19 (18.4%) had CRP < 7.5mg/l and serum albumin < 28g/l suggesting evidence of malnutrition despite low CRP level, while 84 (81.6%) had CRP < 7.5mg/l and serum albumin >28g/l. This shows that there is a negative correlation between CRP and serum albumin levels. OR = 17.68, 95% CI = 1.87 – 16>, P= 0.03. **Conclusion:** Kidney disease is a major risk for malnutrition among patients and correlation between anthropometric indices, serum albumin and CRP will help determine the risk of CKD among patients.

**Keywords:** CKD, malnutrition, risk factors

### INTRODUCTION

Chronic kidney disease (CKD) has a major effect on global health, it is responsible for both direct cause of global morbidity and mortality and as an important risk factor for Malnutrition and cardiovascular disease.[1] CKD is largely preventable and treatable and deserves greater attention in global health policy decision making, particularly among low- and middle-income countries. Chronic Kidney Disease (CKD) is an increasingly common condition worldwide. Generally, it affects less than 1% of the general population<sup>1</sup>. In Nigeria, CKD accounts for 2-8% of total admissions into tertiary Hospital [2,3]. In a 10 years' retrospective study done at Olabisi Onabanjo University Hospital, Sagamu, South-West Nigeria, the frequency of chronic kidney disease in the population was 3.6% (182 of 5,107). Malnutrition is frequently found in patients with CKD before and after dialysis especially in developing economies [4-7] There is paucity of data regarding the prevalence and clinical consequences of protein- energy malnutrition (PEM) among dialysis naïve CKD patients as well as among renal replacement therapy (RRT) and transplant populations. Malnutrition among end stage renal disease (ESRD) population is between 42-72% in developing countries in 42% to 72% and is strongly associated with increased morbidity and mortality [8,9].

Causes of malnutrition in CKD patients include: Inadequate dietary intake of calories and proteins and persistent state of protein catabolism secondary to chronic inflammation [10].

Abnormal metabolism of albumin has also been reported in these patients including redistribution of albumin into the interstitium, decrease synthesis and external loss of albumin [11]. Protein catabolism is further increased in patients undergoing hemodialysis with incompatible membranes. Spontaneous dietary intake of protein and energy tends to decline with renal insufficiency. The calorie intake was significantly higher among patients with fractional Urea clearance (Kt/v) of at least 1.7 and glomerular filtration rate (GFR)  $>0.5\text{mls/min/1.73m}^2$  compared to patients with same Kt/v but with GFR  $<0.5\text{mls/min/1.73m}^2$ . [12] suggesting a clear risk of malnutrition among CKD patients. Malnutrition has been shown to be a risk factor for cardiovascular mortality. In a study done with the aim of assessing the relationship between nutritional indices and cardiovascular mortality among patients with ESRD, it was shown that the risk for cardiovascular death was 39% greater for each 1g/sdl(10g/l) decrement in serum albumin levels. A care provider's assessment of malnutrition was associated with a 27% greater risk for cardiovascular mortality. For one-unit decrement in body mass index (BMI), the risk for cardiovascular disease (CVD) was 6% greater [13].

Patients with CKD are at risk for malnutrition because uremic symptoms (anorexia, nausea, vomiting and altered taste) are superimposed on the restricted diet, malabsorption, and urinary protein losses. This often results in hypoalbuminemia, abnormal profiles of blood amino acid levels, decreased protein and fat stores, and deranged white blood cell function. The institution of appropriate diet or initiation of dialysis therapy may not, however, correct these deficits. It is frequently necessary to enlist the aid of a clinical nutritionist to assist in an aggressive program of enteral or parental nutrition. This includes the careful monitoring of nutritional parameters, such as serum pre-albumin, albumin, and anthropometric measurements of fat and muscle bulk, triceps skinfold thickness and mid-arm muscle circumference). Performance of the subjective global assessment has also become an important tool used to quantify and periodically monitor the nutritional status of CKD patients [14]. This tool has been modified for use in renal failure and is still undergoing revisions and validation in subsets of patients. Currently, brief training is reconsidered for rating the four items (weight change over preceding 6 months, dietary intake and gastrointestinal symptoms, visual assessment of subcutaneous tissue for fat and muscle wasting, and muscle mass) on a seven-point scale.

Clinical and biochemical indices, such as body mass index (BMI), skin fold thickness, serum pre-albumin and albumin, serum cholesterol, total lymphocyte count, and C-reactive protein [15-23] have been used as markers of malnutrition in CKD. However, none of these methods is sufficient on their own in the assessment of malnutrition, hence a combination of methods is used. This study is however intended to correlate biochemical parameters with subjective global assessment (SGA) in the assessment of malnutrition in pre-dialysis CKD patients in north central Nigeria. SGA focuses on gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea), weight loss in the preceding six months in the absence of other causes and visual assessment of subcutaneous tissue and muscle mass [24]. SGA is rated using the SGA rating form. The overall score classification is not simply numerical score. It does strongly depend on the clinical judgment of the examiner. He/ She has to consider whether the patient's status is improving or deteriorating. This information may lead to different "scores" given in each section. The scores are subjectively rated on a four point or seven-point scale [25]. The use of seven-point scale is recommended because of its greater sensitivity and its use in large scale epidemiologic studies such as Canadian United State of America (CANUSA) study [26]. In

CANUSA study, the SGA score was defined as:

Severe malnutrition                      SGA score 1 or 2

Moderate to mild malnutrition              SGA score 3 to 5

Mild malnutrition to normal nutrition SGA score 6 or 7

SGA was found to be related to other markers of nutritional status in dialysis patients [27-29]. From the foregoing therefore, SGA is easy to use and at the same time a cheap way of assessing nutritional status in pre dialysis CKD patients. The high prevalence of malnutrition in CKD ordinarily calls for sophisticated investigations, which offer good prognostic information. Unfortunately, it is impracticable for most physicians caring for patients in settings with limited resources. Malnutrition is established by the usage of anthropometric measurements and biochemical parameters. Biochemical parameters can be used for both diagnostic and prognostic purposes. Determining biochemical parameters is however, very expensive and requires technical expertise. Moreover, it is not readily available in many hospitals in developing countries. Some studies indicate that biochemical parameters correlate with subjective global assessment in assessing malnutrition in CKD. However, there are conflicting reports to that assertion. There is paucity of literature on the correlation of biochemical parameters to subjective global assessment in Nigeria. This study seeks to shed light on the inadequate existing literature and to compare our results with those obtained elsewhere. Correlating biochemical parameters with subjective global assessment may aid in improving the management of chronic kidney disease patients in our environment.

### **STUDY OBJECTIVES**

- To assess the nutritional status among CKD patients using clinical and biochemical parameters
- To determine derangement of some biochemical parameters among CKD patient associated with malnutrition
- To correlate the SGA and Biochemical parameters of malnutrition

### **MECHANISM OF MALNUTRITION IN URAEMIA**

The pathogenesis of protein wasting in CKD is multifactorial. Potential mediators of protein catabolism in chronic uremia include anorexia, low protein-energy intake, increased cortisol and parathyroid secretion, insulin resistance, metabolic acidosis and unidentified uremic toxins<sup>30</sup>. In non-acidotic uremic patients, the rate of protein turnover (that is, synthesis and degradation) has been found to be decreased. Malnutrition also decreases both protein synthesis and degradation. In contrast, during acidosis protein degradation is primarily accelerated and results in rapid loss of body proteins, Cytokine concentrations have often been found increased in both dialyzed and unanalyzed chronically uremic patients.

Studies has shown that the circulating levels of tumor necrosis factor- alpha (TNF - ) and of type I (60KDa) and type II (80KDa) soluble TNF – alpha receptors in unanalyzed uremic patients are greatly increased [30]. In addition, serum creatinine has been shown to correlate with TNF - alpha soluble receptors, thus, TNF –alpha is potentially an important mediator of protein wasting in chronically uremic patients. Pharmacological administration of Pentoxifylline, which

has shown to decrease protein degradation by interfering with the TNF – alpha system (that is, TNF – alpha and its soluble receptors) in experimental models. The prevalence of an increased CRP >6mg/l has been reported to be high in dialysis [31,32] and predialysis patients.[33] Serum levels of CRP appear to reflect generation of pro-inflammatory cytokines, interleukin – 1(IL-1), interleukin -6 (IL-6) and tumor necrosis factor (TNF -) which has been reported to be increased in CKD patients. [34,35] It is well documented that high levels of pro-inflammatory cytokines may cause muscle wasting by stimulating protein catabolism via the ubiquitin proteasome pathway 36 by reducing albumin synthesis and inhibiting appetite [37]. It has also been observed that IL-1, TNF - and endotoxins may induce net catabolism of muscle protein by stimulating branched-chain ketoacid dehydrogenase, which leads to greater oxidation of branched – chain amino acids [38]. In consequence, increased plasma levels of pro-inflammatory cytokines predict hypoalbuminemia [39] and mortality [35,39] in dialysis patients. Furthermore, whereas serum albumin and CRP predict mortality in univariate analysis, only CRP is a significant predictor in multivariate analysis. [40]. Available evidence suggests that increased mortality rate observed in CKD may be associated with an acute-phase response rather than low serum albumin levels caused by other mechanisms.

### **Mortality Risk**

The criteria of malnutrition and its severity degree may be arbitrary in a way that individual patient's data may not fall in only one category. Data showing the correlation between nutritional status and mortality in patients with CKD without renal replacement therapy are rare. Most studies investigate the relation of nutritional status at the beginning of renal replacement therapy and mortality:

- (i) The mortality risk for patients starting dialysis with clinical impression of malnutrition is increased compared to patient without malnutrition [23].
- (ii) Low serum albumin levels at initiation of dialysis are associated with increased mortality. If the patients with serum albumin>4.5 g/dl are taken as reference, the relative mortality risks are 1.7, 3.1. and 5.26 for patients with serum albumin levels of 4.0 – 4.4g/dl. 3.5-3.9g/dl and <3.5g/dl, respectively[62].
- (iii) The SGA at the beginning of dialysis treatment predicts mortality. Steinvickel et al [41] described survival rates of 2 95%, 2 70% and 2 45% after two years in well-nourished mild and moderately malnourished patents respectively.

### **Monitor Every 3-6 Months**

A number of patients may become anorectic during the pre-dialysis period. Therefore, the dietary status should be checked every 3 – 6 months. For slowly progressive nephropathies (e.g., interstitial or reflux nephropathies), this period may be increased, provided the satisfactory data are obtained. For more severe disease, GFR < 20ml/min, concomitant catabolic treatment (steroids), or acute disease, the period between the monitoring visits should be reduced 24.

## **MATERIALS AND METHODS**

This is a cross-sectional study aimed at correlating biochemical parameters to subjective global assessment in determining malnutrition. The study was carried out in Jos University Teaching Hospital (JUTH), a tertiary health institution and referral centre to at least eight neighbouring states. Jos is the capital of Plateau State, north-central Nigeria. It lies between longitude 80' 53'and latitude 90' 56' and covers an area of about 9,400km<sup>2</sup>. It is a cosmopolitan town. The prevalence of malnutrition in North central Nigeria is 43%. The sample size was calculated

using the formula.  $n = \frac{Z^2 Pq}{d^2}$  based on a projected sample size of 58, a sample size of 104 was used for this study to make room for attrition. Our target population was individuals between the ages of 16 – 60 years, Patients with confirmed CKD and those who consented for the study after administering an informed consent. All patients who met the above criteria were recruited for this study. Patients who are on dialysis, with gastrointestinal disease, nephrotic syndrome, severe organ failure, on steroid therapy, active infection and smoking were all excluded from this study. Ethical clearance was sort and obtained from the ethical committee of Jos University Teaching Hospital before commencement.

### DATA COLLECTION

Consecutive patients were interviewed and subjected to the standard questionnaire (Appendix II & III) and the following measurements below were assessed.

#### Anthropometric Measurements

**Height** was recorded with a measurement stand positioned on a flat surface and recorded to the nearest centimeter. Height measurements of patients were taken without shoes.

**Weight** was recorded in kilograms (to the nearest 0.1kg) using a flat scale on a firm horizontal surface with subjects wearing only light clothes and without shoes. The zero mark on the scale was checked before each measurement. Calibration was done by reference on object of known weight before commencement of the study procedure.

The **Body mass index** (BMI) was calculated as weight in kilograms (kg) divided by the square of the height in metres (m<sup>2</sup>).

**Waist circumference** (WC) was measured in centimeters with a dress makers' tape and with the patients wearing minimal clothing as the horizontal level at the mid point between the iliac crest and the lower costal margin.

**Hip circumference** (HP) was measured in centimeters with a dress makers' tape and with the patients wearing minimal clothing as a horizontal level of maximal circumference around the buttocks (posteriorly) and the pubic symphysis (anteriorly). Waist to hip ratio (WHR) was calculated as waist circumference (cm) divided by the hip circumference (cm).

#### Blood Samples

Blood samples were drawn from a forearm vein with the patients seated and relaxed. Samples were put into plain bottles, kept on ice and transported to the chemical pathology laboratory where the plasma was separated from the cells by centrifugation and the plasma was analyzed for serum pre albumin and albumin. Data were analyzed using the SPSS version 2021 statistical program. Means ( $\pm$ SD) were used to describe continuous variable and proportions were used for categorical data. Two tailed students t-test was used for comparisons of group means. When comparing groups of subjects, the chi-squared ( $\chi^2$ ) test was applied to determine the significance of the difference observed. Linear regression analyses were used to determine the relationship between SGA and serum albumin. A p-value of <0.05 is considered significant and p<0.01 highly significant in all statistical comparisons.

#### Statistical Methods

Data were analyzed using the SPSS version 21 statistical program. Means ( $\pm$ SD) were used to

describe continuous variable and proportions were used for categorical data. Two tailed students t-test was used for comparisons of group means. When comparing groups of subjects, the chi-squared (X<sup>2</sup>) test was applied to determine the significance of the difference observed. Linear regression analyses were used to determine the relationship between serum albumin and SGA. A p-value of <0.05 is considered significant and p<0.01 highly significant in all statistical comparisons.

## CHAPTER FOUR: RESULTS

### Age and Sex Distribution

A total of 65 males accounting for 65.2% and 39 females (37.5%) were studied. The mean age of the subjects was  $39 \pm 15$  years with a range of 18 to 62 years. There was no statistically significant difference between the age distribution of the male and female subjects as their mean ages were  $39.5 \pm 14.8$  years and  $39.0 \pm 16.2$  respectively ( $T = 0.16$ ,  $p = 0.8$ ). The highest proportion of subjects was within the age group of 20 to 29 years for both males and females. The proportion of females tended to decrease as age increases while that of males remained relatively stable after the age of 29 years. See Figure 1

■ = males; ■ = females

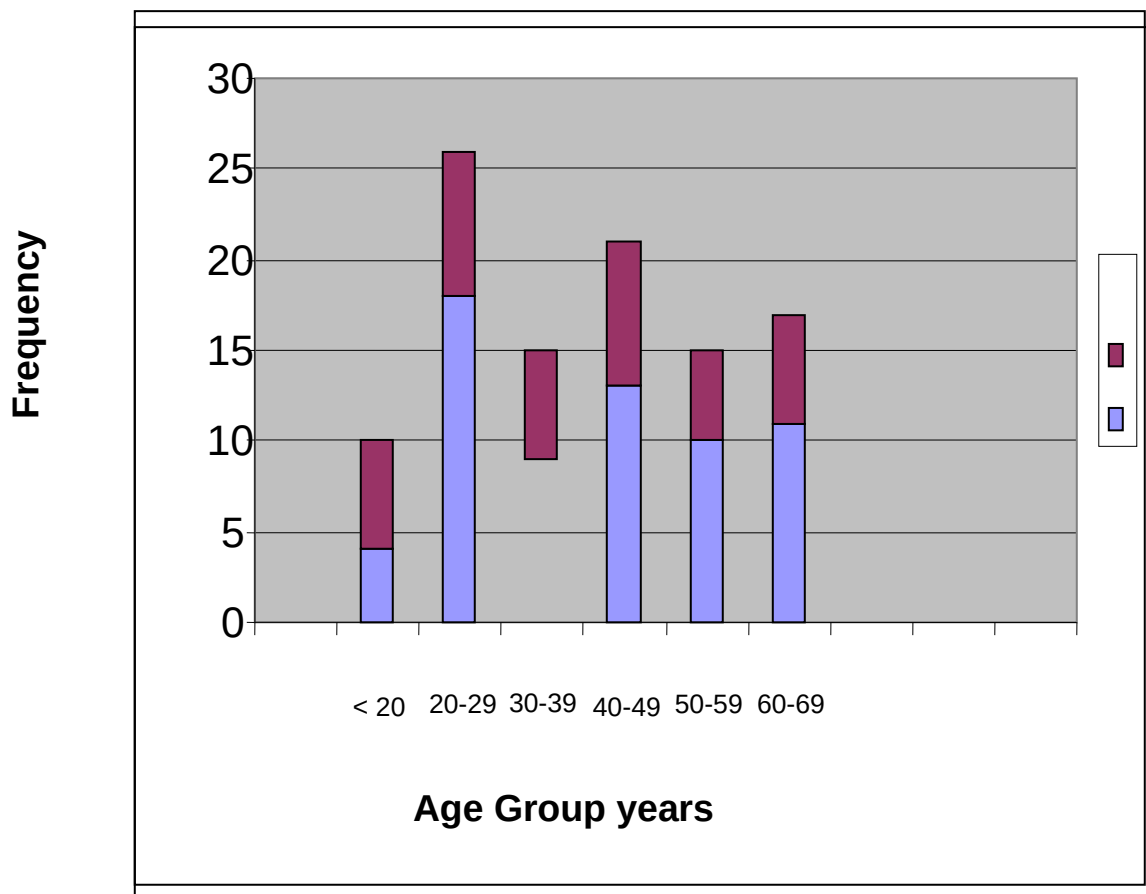


Figure 1. Age and sex distribution of patients with chronic kidney disease

### CHARACTERISTICS OF STUDY SUBJECTS

Patients with chronic kidney disease were studied who are within the age 18 to 62 years. Study groups comprised both males and females.

See table i

**Table i: Characteristics of patients with chronic kidney disease**

| Characteristic                     |                 |
|------------------------------------|-----------------|
| Age, years (mean $\pm$ SD)         | 39.3 $\pm$ 15.2 |
| Sex (M/F)                          | 65/39           |
| Anthropometric indices             |                 |
| BMI, Kg/M2 (mean $\pm$ SD)         | 23.1 $\pm$ 5.0  |
| MAC, cm (mean $\pm$ SD)            | 27.4 $\pm$ 4.4  |
| MAMC, cm (mean $\pm$ SD)           | 46.2 $\pm$ 21.6 |
| TSFT, cm (mean $\pm$ SD)           | 12.5 $\pm$ 7.2  |
| <b>Laboratory parameters</b>       |                 |
| PCV, % (mean $\pm$ SD)             | 28.0 $\pm$ 7.9  |
| FBS, mmol/L (mean $\pm$ SD)        | 5.7 $\pm$ 2.8   |
| SCR, $\mu$ mol/L (median)          | 807.5           |
| GFR, ml/min (median)               | 9.9             |
| UPCR, mg/mg (median)               | 0.8             |
| CRP, mg/L (median)                 | 0.75            |
| TG, mmol/L (mean $\pm$ SD)         | 1.4 $\pm$ 0.7   |
| TC, mmol/L (mean $\pm$ SD)         | 4.9 $\pm$ 1.2   |
| HDL, mmol/L (mean $\pm$ SD)        | 0.95 $\pm$ 0.28 |
| Total protein, g/L (mean $\pm$ SD) | 68.2 $\pm$ 10.4 |
| Albumin, g/L (mean $\pm$ SD)       | 33.1 $\pm$ 6.7  |
| SGA (mean $\pm$ SD)                | 3.9 $\pm$ 1.5   |

## Anthropometric Indices

### Body Mass Index:

The body mass index (BMI) of the subjects has a mean of  $23.3 \pm 5.0$  Kg/M2. The mean BMI of the females was higher than that of the males though not statistically significant ( $24.5 \pm 6.4$  vs.  $22.6 \pm 3.7$  Kg/M2 respectively;  $T = 1.92$ ,  $p = 0.06$ ).

### 4.2.3.2

### Mid - Upper Arm Circumference (MUAC):

The MUAC of the subjects ranged from 19 to 38 cm with a mean of  $27.4 \pm 4.4$  cm. The MUAC was similar in males and females being  $27.1 \pm 3.9$  cm and  $27.9 \pm 5.1$  cm respectively;  $T = 0.94$ ,  $p = 0.34$ .

### Mid-Arm Muscle Circumference (MAMC):

The mean MAMC was  $46.2 \pm 21.6$  cm. The MAMC was higher in males compared to females being  $51.5 \pm 21.1$  and  $38.6 \pm 19.0$  cm respectively,  $T = 3.14$ ,  $p = 0.002$ .

### Triceps Skin Fold Thickness (TSFT):

The median TSFT was 11.5 cm with a range of 2 cm to 29 cm. The median values for females is twice that of the males (16 cm vs. 8 cm respectively; Kruskal-Wallis H (equivalent to chi-square) = 14.39,  $p = 0.0001$ ).

### Serum Albumin:

The serum albumin ranged from 21 to 47 g/L with a mean of  $33.2 \pm 6.4$  g/L. It was similar in both sexes ( $33.5 \pm 6.1$  g/L for males and  $32.5 \pm 6.9$  g/L for females respectively,  $T = 0.73$ ,  $p =$

0.46).

### Urinary Protein Creatinine Ratio (UPCR):

The median for both sexes was 0.80 mg/mg with a range of 0.02 mg/mg to 2.7 mg/mg. The median values were 0.7 mg/mg and 0.9 mg/mg in males and females respectively; Krustal-Wallis H = 1.92; p = 0.16.

### Renal Function:

#### Serum Creatinine

- The median serum creatinine of the subjects was 807.5  $\mu\text{mol/L}$  with a range of 71 to 2326  $\mu\text{mol/L}$ . The median values for male and female subjects were 596  $\mu\text{mol/L}$  and 943  $\mu\text{mol/L}$  respectively. This difference however was not statistically significant (Kruskal – Wallis H = 3.04, p = 0.08).
- Glomerular Filtration Rate (GFR) The median glomerular filtration rate (GFR) was 9.9 ml/min/1.73m<sup>2</sup> with a range of 2.1 to 121.4 ml/min/1.73m<sup>2</sup>. The median values for males and females were 10.8 and 7.9 ml/min/1.73m<sup>2</sup> respectively; Kruskal – Wallis H = 8.61, p = 0.003. Table 2 shows the distribution of the subjects according to the stage of chronic kidney disease using the GFR. The majority (90.5%) of the subjects had GFR < 60 ml/min/1.73m<sup>2</sup> with more than half of the subjects (63.6%) in stage 5. See table ii

**Table ii: Stages of chronic kidney disease patients**

| STAGE | GFR       | %    |
|-------|-----------|------|
| 1     | $\geq 90$ | 3.8  |
| 2     | 60 – 89   | 5.7  |
| 3     | 30 – 59   | 10.5 |
| 4     | 15 – 29   | 16.4 |
| 5     | < 15      | 63.6 |

GFR = Glomerular filtration rate

### Subjective Global Assessment (SGA)

The mean SGA of the subjects was  $3.95 \pm 1.57$ . For males, it was  $4.03 \pm 1.63$  while for females the mean was  $3.82 \pm 1.50$ . The P value is 0.51 signifying that there is significant statistical difference.

### Inflammation

The median CRP was 0.75 mg/L for both males and females respectively. Seven subjects (6.7%) had evidence of inflammation (i.e., CRP > 7.5 mg/L).

CI = 0.22 – 1.47 and P = 2.24. There is also no relationship between sex and serum albumin level.

### Relationship between Markers of Malnutrition and Aetiology of Malnutrition

- Relationship Between BMI and Cause of CKD (Diabetics Versus Non-Diabetics). There were 9 (31%) of diabetics versus 5 (6.3%) of non-diabetics had low BMI. OR = 6.6, 95% CI = 2.00 – 22.10; P = 0.0001. Thus, being diabetic confers a worse risk for low BMI. See table iii

**Table iii: Relationship between BMI and Causes of CKD Diabetes Mellitus**

|                         | Yes      | No         |
|-------------------------|----------|------------|
| BMI                     |          |            |
| <18.5kg/m <sup>2</sup>  | 9 (31%)  | 5 (6.3%)   |
| > 18.5kg/m <sup>2</sup> | 20 (69%) | 70 (93.7%) |

OR > 6.6, 95% CI = 2.00 – 22.10, P = 0.0001

### **Relationship Between Serum Albumin and Causes of CKD (Diabetes Versus Non-Diabetics)**

This Indicates that 7 (24.1%) of diabetic had low albumin below 28g/l as compared with 16 (23%) of non-diabetics. OR = 1.25, 95% CI = 0.45 – 3.45, P = 0.6. Thus, there is no significant association between cause of CKD and Prevalence of hypoalbuminemia. See table iv

**Table iv: Relationship between serum albumin and cause of CKD (diabetic /non diabetic) Diabetes Mellitus**

|               | Yes-       | No         |
|---------------|------------|------------|
| Serum albumin |            |            |
| <28g/l        | 7 (24.1%)  | 16 (20.3%) |
| > 28g/l       | 22 (75.9%) | 59 (79.7%) |

OR = 1.25, 95% CI = 0.45-3.4, P = 0.6

- Relationship Between SGA and Cause of CKD (Diabetics/ Non-Diabetics) 23 (79.3%) of diabetics had SGA <6 compared to 56 (70.9%) of non diabetics. OR = 1.57, 95% CI = 0.56 – 4.37, P = 0.38. There is therefore no significant association between being diabetic and being malnourished as detected by SGA. See table v

**Table v: Relationship between SGA and cause of CKD (diabetics vs non-diabetics) Diabetes Mellitus**

|     | Yes        | No         |
|-----|------------|------------|
| SGA |            |            |
| <6  | 23 (79.3%) | 56 (70.9%) |
| >6  | 6 (21.7%)  | 19 (29.1%) |

OR = 1.57, 95% CI = 0.56 – 4.37, P = 0.38.

### **Correlation between Serum Albumin and Subjective Global Assessment**

There exists no liner relationship between serum albumin to SGA. The  $r^2 = 0.11$  which indicates that a change in albumin contributes only 11% to a change in SGA. However, when SGA of less than 6 is compared with albumin level of less than or equal to 28g/l, 25(89.3%) had hypoalbuminaemia with SGA less than 6 while 3 (10.7%) had hypoalbuminaemia but SGA was above 6. 54 (67.5%) had no hypoalbuminaemia but had SGA less than 6 and 26 (32.5%) had no hypoalbuminaemia and SGA above 6. The odds ratio is 4. 01 with confidence interval 1.10 to 14.51 and a P value of 0.01. This shows that there is a good relationship between the performance of hypoalbuminaemia and SGA in detecting malnutrition see table vi

**Table vi: Comparison between serum albumin and subjective global assessment in detecting malnutrition Subjective Global Assessment**

|               | <6    | >6    |
|---------------|-------|-------|
| Serum albumin |       |       |
| <28g/l        | 89.3% | 10.7% |
| >28g/l        | 67.5% | 32.5% |

OR = 4.01, 95% CI 1.10 – 14.51 P = 0.01.

**Correlation between Serum Albumin and C- Reactive Protein**

Within the study subjects there were 4 (80%) of patients with CRP >7.5mg/l had serum albumin level of <28g/l. 1 (20%) has CRP >7.5mg/l but serum albumin was > 28g/l. 19 (18.4%) had CRP < 7.5mg/l and serum albumin < 28g/l while 84 (81.6%) had CRP < 7.5mg/l and serum albumin >28g/l. OR = 17.68, 95% CI = 1.87 – 167, P = 0.03. This shows that there is a negative correlation between CRP and serum albumin levels. See table vii

**Table vii: Correlation between serum albumin and C-reactive protein Serum Albumin**

|          | <28g/l     | >28g/l     |
|----------|------------|------------|
| CRP      |            |            |
| >7.5mg/l | 4 (80%)    | 1 (20%)    |
| <7.5mg/l | 19 (18.4%) | 84 (81.6%) |

OR = 17.68, 95% CI = 1.87 – 167 P = 0.03

**Correlation between Subjective Global Assessment and C- Reactive Protein**

There were (80%) of these with CRP > 7.5mg/l had SGA <6 while 1 (20%) of these with CRP > 7.5mg/l had SGA > 6. 75 (72.8%) had CRP < 7.5mg/l with SGA <6 and 28 (27.2%) had CRP < 7.5mg/l and SGA >6. OR = 1.49, 95% CI = 0.15 – 13.94, P = 0.6. There is therefore no relationship between SGA score and level of CRP. See table viii

**Table viii: Correlation between Subjective global assessment and C-Reactive Protein. Subjective Global Assessment**

|          | <6         | >6         |
|----------|------------|------------|
| CRP      |            |            |
| >7.5mg/l | 4 (80%)    | 1 (20%)    |
| <7.5mg/l | 75 (72.8%) | 28 (27.2%) |

OR = 1.49, 95% CI = 0.15 – 13.94, P = 0.6.

**DISCUSSION AND CONCLUSION**

Several clinical and biochemical parameters have been used as markers of malnutrition. These includes: anthropometric, body mass index (BMI), skin fold thickness, serum pre-albumin, serum albumin, cholesterol, total lymphocyte counts and C-reactive protein [15-23].

Application of all these methods is often impracticable in a society like ours because of limited resources and the unavailability of a number of these tests in many of our hospitals. The findings from this study therefore, provides prevalence of malnutrition based on BMI, serum albumin and subjective global assessment and the correlation between these methods.

The prevalence of malnutrition based on BMI was found to be 13.0%. This is lower than an earlier finding by Agaba et al. [9] who reported a prevalence of 21.6% in Jos, North Central Nigeria. This difference might be due to the lower cut off for the BMI used in our study. Agaba et al used BMI less than 20kg/m<sup>2</sup> while this study used the BMI of less 18.5kg/m<sup>2</sup>. Another possible reason of this difference may be that relatively small number of patients were used in their study. The prevalence in this study is also lower than the those found by Huidobro et al [42] in Chile who reported 38%. Siddiqui et al [43] reported a prevalence of 37.5% in Rawalpindi, India. Kumar et al [10] reported a prevalence of 40% in Karachi, Pakistan. Dry weight was not taken into consideration in these studies similarly the number of patients studied, difference in diet, life style, ethnic characteristics and degree of renal failure might have accounted for the difference in prevalence between these studies.

### **Prevalence of Malnutrition**

Based on the BMI the pragmatic approach is that those with BMI below 18.5 kg/m<sup>2</sup> are said to be malnourished. In this study 14 (13.0%) were found to have BMI below 18.5 kg/m<sup>2</sup>.

Based on Serum albumin level of  $\leq 28$ g/l which was used as the cut off point for malnutrition. 28 (25.9%) were found to have serum albumin below 28g/l.

Using the SGA to assess malnutrition, those that have SGA score of 1 or 2 are said to be severely malnourished, while those that have scores of between 3 to 5 are mild to moderately malnourished. It was found that 79% (73.1%) were found to have SGA score of below 6.

When sex and low BMI was matched, the prevalence of Malnutrition Relationship Between Sex and Low BMI was 8 (12.3%) of males and 6 (15.4%) of females had BMI < 18.5kg / M<sup>2</sup> with an odds ratio (OR) = 0.77, 95% confidence interval (CI) 0.24 – 2.41 and P = 0.68 suggesting that there is no relationship between sex and low BMI.

The relationship Between Sex and SGA showed 48 (73.8%) of males and 31 (79.5%) of females had SGA below 6 with OR = 0.72, 95% CI = 0.28 – 1.89 and P = 0.51. this study showed that there is no significant relationship between sex and malnutrition based on the SGA.

Similarly, when Sex and Albumin was matched, we found that 12 (18.5%) of males and 11 (28.2%) of females had serum albumin levels below 28g/l with OR = 0.57, 95% Based on serum albumin we found that malnutrition was seen in 25.9% of patients based on serum albumin. This figure of 25.9% compares with the reported in western countries where 10 to 54% was reported 5,6,7. similarly Agaba et al [9] reported a prevalence of 43% and In a study by Siddiqui et al [43] in Rawalpindi, India however, a prevalence of 90.6% was found but that study used serum albumin cut off of less than 40g/l.

Similarly, the prevalence of malnutrition based on SGA was found to be 76% in this study. This compares to other studies done by Steiber et al [44], Julien et al [45], Tayyem et al [46], who reported a prevalence of 71%, 76%, and 75% respectively. Epinosa et al [47] found the prevalence of 76% in males and slightly higher prevalence of 86% in females. However, our findings are higher than the studies by Visser et al [48] who reported a prevalence of 36%, Tapiawala et al [49] reported a prevalence of 48%, Tayyem et al [46] reported 61.8% and

Lawson et al [9] reported 28%. The lower prevalence reported by these authors may be due to the fact that patients in early stages of renal failure might have been studied. Another possibility is that compliance to medication is good in developed societies unlike our own environment. Since SGA is based on clinical parameters, prevalence of malnutrition is likely to be lower in people who are compliant with medication since they are more likely to be less symptomatic.

When SGA was correlated with serum albumin, we found 25 (89.3%) of patients with SGA of less than 6 with albumin level of less than 28g/dl. Though there is no linear relationship between serum albumin and SGA ( $r^2 = 0.11$ ), but this study shows the good relationship between the performance of serum albumin and SGA in detecting malnutrition. This result agrees with the work done by Visser et al [48] who showed a lower correlation of SGA scores to serum albumin levels. This assertion is also in keeping with the work reported by Tapiawala et al [49] who showed that dietary protein and Calorie intake and serum albumin levels did not correlate well with the SGA scores. In another report by Lawson et al [5] no correlation between SGA and serum albumin was found. Although SGA scores in most studies did not show good relationship between serum albumin, studies above demonstrated that it is a veritable way of detecting malnutrition in CKD patients and thus can be used as a screening tool for malnutrition.

This study showed that 80% of those who have malnutrition based on our evidenced by serum albumin below 28g/dl also had on going inflammation (CRP of  $>7.5\text{mg/l}$ ). This finding is similar to the report by Siddiqui et al [43] who found that in 35.9% of patient who had elevated CRP had a lower mean serum albumin than those who had a normal CRP ( $32.7\text{g/l}$  vs  $35.4\text{g/l}$ ) which was statistically significance ( $P = 0.017$ ). In a study by Perunicic et al [50], there was a negative correlation between serum albumin concentration and inflammatory markers ( $r = 0.31$ ,  $P = 0.05$ ). Suliman et al [51] also found out that the patients with inflammation [C-reactive protein (CRP) concentrations  $>10\text{mg/l}$ ] or malnutrition had lower amino acid concentrations than did the patients with no inflammation or malnutrition the presence of both inflammation and malnutrition was associated with more marked reductions in amino acid concentrations than malnutrition alone. Menon et al [52] also found out that CRP level was inversely related to albumin level.

Most studies have shown inverse relationship between CRP levels and serum albumin. Protein-energy malnutrition PEM and inflammation are common in patients with chronic kidney disease (CKD) and worsen as the CKD progresses towards the end stage renal disease (ESRD). As such one must exclude inflammation when using serum albumin for detecting malnutrition. This study also showed that 80% of those who had subjective global assessment below 6 had C-reactive protein  $> 7.5\text{mg/litre}$  ( $p=0.6$ ). This study did not show any significant relationship between SGA and CRP. Similar findings was reported Steinkel et al [33] who reported that 72% of patients with inflammation had uremic malnutrition by SGA. Quresh et al [53] reported a similar observation. He reported that those with malnutrition determined by SGA had about four-fold higher prevalence of inflammation. Jenin et al [29] found a high positive correlation of SGA with CRP. On the contrary, Abdallah et al [53] reported a lower prevalence of 65%.

Similarly, when we correlated between SGA and BMI, we found that 20% of those with SGA score less than 6 had a BMI of  $<18.5\text{kg/m}^2$ . This study did not show significant relationship ( $p = 0.5$ ) between SGA and BMI. Kalantar-Zadeh et al [54] showed that SGA had no significant relationship with BMI. Contrary to the finding in this study, Visser et al [48] reported a strong

relationship between SGA scale and BMI ( $r = 0.79$ ,  $p < 0.01$ ). Jerin et al (34 reported that the rates of malnutrition defined by SGA method showed a high negative correlation with BMI.

### **CONCLUSIONS AND RECOMMENDATIONS**

Malnutrition is common in CKD patient therefore patient should be routinely screened for malnutrition and it causes treated.

None of the markers of malnutrition can be used as a single entity in detecting malnutrition such parameters should always be correlated with each other Serum albumin can be used as a marker for malnutrition only when inflammation is adjusted for, detection of malnutrition by SGA correlates with hypo-albumineamia and thus SGA could be used as a veritable tool for detecting malnutrition.

### **LIMITATIONS OF THE STUDY**

- Other causes of malnutrition like GI disease, malignancies etc were not looked into
- Since subjective global assessment is based on history and physical examination, correct response might not be obtained from some patients. Most patient do not know their previous weight so it was difficult to determine what amount of weight that has been lost in the preceding six months.
- Serum pre-albumin, one of the biochemical parameters was not assayed as it is not routinely carried out in must developing countries.
- Serum lipids were not used in the correlation of SGA as only 4.8% of all patients studied have serum lipids below normal levels.
- Prevalence of malnutrition using BMI, hypo-albumineamia and SGA in the various stages of CKD was not assessed as more than 60% of the patients were in stage V, thus making statistical analysis not possible.

### **Conflict of Interest**

This research has ethical approval from the management of Jos university Teaching Hospital, Plateau state.

There is no conflict of interest nor funding received from any source or organisations for the purpose of this research.

### **Abbreviations**

1. Chronic kidney disease CKD
2. Diabetes mellitus (DM)
3. Subjective global assessment (SGA),
4. Body mass index (BMI)
5. waist circumference (WC)
6. Hip circumference (HC)
7. Mid-Arm Muscle Circumference (MAMC)
8. Triceps Skin Fold Thickness (TSFT)
9. Urinary Protein Creatinine Ratio (UPCR)
10. C-reactive protein (CRP)
11. Packed cell volume (PCV)
12. Full blood count (FBS)

13. Serum creatinine (SCR)
14. Triglyceride (TG)
15. Total Cholesterol (TC)
16. High density lipoprotein (HDL)
17. Low density lipoprotein (LDL)
18. Renal replacement therapy (RRT)
19. End stage renal disease (ESRD)
20. Glomerular filtration rate (GFR)
21. Canadian United State of America (CANUSA)
22. Tumor necrosis factor- alpha (TNF - )
23. Interleukins (IL)
24. Jos University Teaching Hospital (JUTH)
25. chi-squared (X2)
26. Statistical package for the social sciences (SPSS)

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