Nutritional Markers in Patients Undergoing Chronic Haemodialysis in Jamaica

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ABSTRACT

Objectives: *The main objective of the study is to assess the nutritional status in patients on chronic haemodialysis in Jamaica using the Subjective Global Assessment tool and to correlate this with measured serum nutritional biomarkers, and also to identify nutritional biomarkers that can be used to assess nutritional status of patients with end-stage renal disease (ESRD).*

Subject and Methods: *Two hundred and nine consecutive patients on haemodialysis were selected from dialysis centres in Kingston, the capital of Jamaica, St Catherine and Manchester, Jamaica. The nutritional status of each participant was assessed using the Subjective Global Assessment tool in an interview performed by the researcher. Serum albumin, blood urea nitrogen and creatinine, highly sensitive complement reactive protein (hsCRP) and total fasting cholesterol were determined from a single serum sample. Only patients with ESRD were selected. Patients with acute renal failure or those with ESRD who were admitted in the previous two weeks were excluded from the study. Informed consent was obtained prior to interview and obtaining blood samples.*

Results: *Of the total participants, 54.5% (n = 114) were male and 45.5% (n = 95) female. The mean age for males was 51.9 years and females 47.6 years. Diabetes was documented as the most common cause of chronic renal disease and was found in 29.7%, hypertension in 24.4% and chronic glomerulonephritis in 22% of the participants. Approximately 80% of the study population had moderate malnutrition. There was a significant association between moderate malnutrition and a diagnosis of ESRD secondary to diabetes mellitus,* $p = 0.03$. *Being on haemodialysis for ≤ six months was significantly associated with moderate malnutrition* $p = 0.002$. *Also associated with moderate malnutrition were presence of an arteriovenous (AV) fistula (p = 0.01), serum albumin of < 40 g/L (OR 3.68,* $p = 0.001$*), pre-dialysis creatinine of < 880 µmol/L (*$p = 0.02$*) and cholesterol < 3.9 mmol/L (*$p = 0.04$*). Highly sensitive complement reactive protein levels of > 10 mg/L was associated with moderate malnutrition, though statistical signifance was not met (*$p = 0.39$*).*

Conclusion: *Factors associated with malnutrition in patients on dialysis were having ESRD secondary to diabetes mellitus, dialysis duration for ≤ six months, low serum albumin, pre-dialysis serum creatinine of 880 µmol/L, low total cholesterol and presence of AV fistula access.*

Keywords: Chronic haemodialysis, nutritional markers, patients

Marcadores Nutricionales en Pacientes en Hemodiálisis Crónica en Jamaica

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RESUMEN

Objetivos: *El objetivo principal del estudio es, por una parte, evaluar el estado nutricional en pacientes en hemodiálisis crónica en Jamaica, usando como herramienta la Valoración Global Subjetiva (VGS),*

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y por otra parte, poner en correlación los datos con la medición de los biomarcadores nutricionales séricos, identificando a la par los biomarcadores nutricionales que pueden usarse para evaluar el estado nutricional de pacientes con enfermedad renal en etapa terminal.

Sujetos y Métodos: *Se seleccionaron doscientos nueve pacientes consecutivos en hemodiálisis de los centros de diálisis en Kingston, la capital de Jamaica. El estado nutricional de cada participante fue evaluado usando la Valoración Global Subjetiva como herramienta, en una entrevista realizada por el investigador. La albúmina en suero, el nitrógeno ureico y la creatinina en sangre, la proteína C-reactiva altamente sensible (hsCRP), y el colesterol total en ayunas, fueron determinados a partir de una sola muestra de suero. Sólo se escogieron pacientes con la enfermedad renal en etapa terminal (ERET). Los pacientes con insuficiencia renal aguda o aquellos con ERET ingresados en las dos semanas previas, fueron excluidos del estudio. Se obtuvo consentimiento informado antes de la entrevista y la toma de muestras de sangres.*

Resultados: *Del total de participantes, 54.5% (n = 114) fueron varones y 45.5% (n = 95) fueron hembras. La edad promedio de los varones fue 51.9 años y la de las hembras 47.6 años. La diabetes se documentó como la causa más común de la enfermedad renal crónica, y se halló en 29.7%. Asimismo, se evidenció hipertensión en 24.4% y glomerulonefritis crónica en 22% de los participantes. Aproximadamente el 80% de la población en estudio presentaba desnutrición moderada. Hubo una asociación significativa entre la desnutrición moderada y un diagnóstico de ERET secundario de diabetes mellitus,* p = *0.03. El hallarse en hemodiálisis por ≤ seis meses estuvo significativamente asociado con desnutrición moderada,* p = *0.002. Asimismo, asociados con la desnutrición moderada estuvieron la presencia de una fístula arteriovenosa (AV) (*p = *0.01), albúmina en suero de < 40 g/L (OR 3.68,* p = *0.001), creatinina pre-diálisis de < 880 µmol/L (*p = *0.02), y colesterol < 3.9 mmol/L (*p = *0.04). La proteína C-reactiva altamente sensible (hsCRP) en niveles > 10 mg/L, estuvo asociada con la desnutrición moderada, aunque sin alcanzar significación estadística (*p = *0.39).*

Conclusión: *Los factores asociados con la desnutrición en los pacientes de diálisis fueron la ERET secundaria a la diabetes mellitus, duración de la diálisis ≤ seis meses, baja albúmina en suero, creatinina sérica pre-diálisis de 880 µmol/L, bajo colesterol total, y la presencia de acceso mediante una fístula AV.*

Palabras claves: Hemodiálisis crónica, marcadores nutricionales, pacientes

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INTRODUCTION

Moderate and severe malnutrition is endemic in much of the developing countries (1). The presence of low socio-economic status can negatively impact on well-being of the population, and more so in those with chronic diseases. Malnutrition affects up to 75% of patients with end-stage renal disease (ESRD). Malnutrition begins as renal function decreases, and patients with chronic kidney disease (CKD) are known to have a progressive decrease in both protein and total caloric intake as glomerular filtration rate decreases (2). The nutritional requirements of patients with worsening kidney function are altered and sometimes lead to ineffective energy production despite adequate intake of protein and carbohydrate substrates. This is because malnutrition in chronic renal failure is due to multiple factors such as metabolic acidosis, hormonal changes, co-morbidities and hospitalizations, dialytic nutrient losses, dialysis-induced catabolism and infection in addition to inadequate protein/caloric intake and increased energy expenditure. There is adequate evidence to suggest that poor nutritional status prior to dialysis increases patient morbidity and mortality after initiating renal replacement therapy [RRT] (3).

Decreased intake of protein and calories is a major contributor to malnutrition in renal failure (3, 4). Maintenance of a neutral nitrogen balance is therefore important for the preservation of nutritional health in patients with chronic renal impairment. Patients with a glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2 should undergo assessment of dietary protein and energy intake and nutritional status (4). Pre-dialysis patients with protein intake of < 0.7 g/kg/day may already have malnutrition originating prior to initiating RRT. A low protein intake of less than 0.75 g/kg/day is an early warning sign for the development of uraemic malnutrition. It has been demonstrated that nutritional markers, serum albumin and creatinine improve during the first half year of haemodialysis (3–5), implying that there is an improvement in nutritional status after initiation of dialysis.

There is no single measurement of malnutrition. Several nutritional markers can be used to assess the nutritional status of renal failure patients. Serum albumin is a re-

liable indicator of visceral protein and is the most extensively studied of the nutritional markers. Low levels of serum albumin are highly predictive of poor clinical outcomes in all stages of CKD and, therefore, serum albumin is considered a reliable marker of general clinical status (5, 6). However, non-nutritional causes of hypoalbuminaemia, such as tissue injury, hepatic disease, renal losses, gastrointestinal disorders and volume overload, can affect the specificity of this marker.

Serum pre-albumin (transthyretin) is a sensitive marker for assessing subtle changes in visceral protein stores due to its low body pool and fairly rapid turnover of two to three days. Levels < 30 mg/dL suggest protein depletion. Pre-albumin levels are inversely related to mortality (7).

The half-lives of pre-albumin, transferrin and retinol binding protein are considerably shorter than that of albumin, therefore changes in nutritional status will be reflected more promptly in levels of these three than in albumin (8). These proteins act as negative acute-phase reactants, *ie* their serum concentrations decrease in response to systemic inflammation and in a roughly proportional degree to the severity of the inflammatory response. This effect severely curtails their reliability as indicators of protein energy malnutrition in the acutely ill patient.

Blood urea nitrogen (BUN) and creatinine are also simple markers of nutritional status. Patients with stage 5 CKD in whom the serum creatinine concentration is < 880 µmol/L (< 10 mg/dL) should be evaluated for muscle wasting as a result of poor nutrition. Also, serum cholesterol concentrations less than 150 mg/dL (3.9 mmol/L) can indicate low levels of dietary and energy intake. Low or declining serum total cholesterol levels are predictive of an increased mortality risk.

Several studies suggest that serum insulin growth factor-1 (IGF-1) concentrations may have a better correlation with body composition than serum albumin and transferrin. However, at the present time, the level of IGF-1 at which malnutrition is significant has not been established in haemodialysis patients (7). Additionally, in a study of 176 patients with ESRD, interleukin (IL-6) and hsCRP levels were independently associated with malnutrition whilst serum albumin was not (9). Interleukin, serum albumin and fetuin A, however, better predicted mortality in multivariate analyses (9).

There is a strong association between malnutrition, inflammation and atherosclerosis (MIA syndrome) in patients on dialysis and those with chronic kidney disease (10). This suggests that chronic inflammation leads to accelerated atherosclerosis and malnutrition. Inflammation is defined as elevated hsCRP above 5–10 mg/L. There is, however, no consensus with regard to the optimal "cut-off" point of CRP used to define the presence of inflammation in CKD patients (11).

The analysis of a patient's body composition also provides important nutritional information. Malnutrition associated with obesity is closely related to morbidity and mortality in the dialysis population possibly due to the increase in visceral fat. Anthropometric studies (oedema-free weight, body mass index (BMI), assessment of arm fat and muscle) have been used to estimate body composition and nutritional adequacy. However, reproducibility of anthropometric measurement is poor and is dependent upon the skill of the observer (3). It has been found to be unreliable in the haemodialysis setting.

The Subjective Global Assessment (SGA) is a rapid and inexpensive nutritional assessment tool that can adequately assess nutritional status in patients on dialysis (peritoneal and haemo). It is a comprehensive tool that uses several components of a medical history, such as weight change, dietary intake, gastrointestinal symptoms, functional capacity and nutritional requirement and relation to disease. It can give an overview of nutritional intake and body composition, including a rough assessment of both muscle mass and fat mass, and it correlates with mortality rates. A focussed history and physical examination are used to categorize patients as well nourished (category A), having mild or moderate malnutrition (category B), or having severe malnutrition (category C). Despite the subjective nature of some of its components, there is excellent agreement between independent observers (12–14).

Nutritional assessment in patients with CKD/ESRD is an important vital aspect in the provision of quality care in this population (15–19). Early detection using reliable parameters by healthcare providers should be embarked on in order to prevent or regress malnutrition in CKD/ESRD (20). There have been no studies looking at these parameters in the CKD/ESRD population in the Caribbean. Therefore, the objectives of this study were to: (a) assess the nutritional status in chronic haemodialysis patients in Jamaica using the Subjective Global Assessment tool and correlate this with measured serum nutritional biomarkers and (b) identify parameters that can be used to assess nutritional status of CKD/ESRD patients in Jamaica.

SUBJECTS AND METHOD

Two hundred and nine consecutive patients on chronic haemodialysis (end-stage renal failure) were selected from dialysis centres in Kingston, St Catherine and Manchester, Jamaica. Written consent was obtained for participation in the study. Patients with acute renal failure or those with ESRD who had been admitted to hospital in the previous two weeks were excluded from the study.

Subjects selected had nutritional status assessed by the researcher using the Subjective Global Assessment tool in an interview. Age, height and weight, type of access and diagnoses were recorded. A blood sample of no more than 10 ml was taken for serum albumin, electrolytes, BUN and creatinine, hsCRP and total fasting cholesterol.

The data were analysed using Microsoft Excel and Epi Info™ software. Univariate and bivariate analyses were

performed and appropriate *p*-values and odd ratios calculated, *eg* the malnutrition status was compared to albumin, pre-dialysis creatinine, cholesterol, BMI, ESRD secondary to diabetes mellitus and hypertension.

RESULTS

Two hundred and nine consecutive patients were selected, 54.5% (n = 114) were male and 45.5% (n = 95) female. Most of the patients were 40 to 70 years old. The mean age for males was 51.9 years and females 47.6 years (Table). There

Table: Demographic distribution, body mass index (BMI), cause of end-stage renal disease and nutritional status

Parameters	Percentage of Patients (n = 209)
Gender M/F	54.5/45.5
Mean age M/F	51.9/47.6
Body mass index M/F	25.1/25.2
Underweight	8.1
Normal	42.6
Overweight	30.6
Obese	15.8
Not assessed	2.9
Cause of ESRD	
Chronic glomerulonephritis	22.0
Diabetes mellitus	29.7
Hypertensive nephrosclerosis	24.4
Autosominal dominant polycystic kidney disease	4.8
Sickle cell associated nephropathy	1.4
Lupus nephritis	5.7
HIV related nephropathy	2.9
Others	9.1
Nutritional status (using SGA)	
Well nourished	19.6
Moderate malnutrition	80.0
Severe malnutrition	1.4

was no difference between mean BMI between males and females, 25.1 kg/m^2 and 25.2 kg/m^2, respectively. However, BMI was slightly higher in diabetics (26.9 kg/m^2) compared to non-diabetics (24.5 kg/m^2). Demographic data showed that 45% of the participants lived in Kingston, 26.8% in St Catherine, 5.2% in May Pen, 3.3% in St Ann and 19.6% from other parishes.

Diabetes was the most common cause of chronic renal disease and was found in 29.7% of the participants, hypertension in 24.4% and chronic glomerulonephritis (CGN) accounted for 22%. Lupus nephritis was present in 5.7%, adult polycystic kidney disease (APKD) in 4.8%, HIV-associated nephropathy in 2.9% and sickle cell nephropathy in 1.4%. Other causes of ESRD accounted for 9.1% of the participants.

Participants on dialysis for up to one year were 38.3% of the study population. Approximately 45% of the participants were on dialysis for one year to five years and 18.7% of the participants were on dialysis for > five years. Being on dialysis for less than or equal to six months was significantly associated with moderate malnutrition, $p = 0.002$.

Those with an arteriovenous (AV) fistula were 45.5% whilst 40.7% had a permanent internal jugular catheter, 4.3% had a temporary subclavian catheter, 3.8% had a temporary internal jugular catheter and 2.4% had a permanent femoral catheter. Only 14.5% of those on dialysis for up to six months had an AV fistula. Presence of an AV fistula was significantly associated with moderate malnutrition, $p = 0.01$, whilst pre-sence of a permanent internal jugular catheter was associated with malnutrition, $p = 0.05$.

Body mass index was defined using the World Health Organization classification. Patients with a normal BMI accounted for 42.6% of the population, 30.6% were overweight, 15.8% were obese and 8.1% were underweight; 2.9% of patients were not assessed. Approximately 80% of the population had moderate malnutrition as assessed by the SGA. Severe malnutrition was seen in 1.4% and 19.6% were well-nourished. Overweight or obesity was present in 34.5% who also had moderate malnutrition. A low BMI was not significantly associated with moderate malnutrition (RR 1.19, $p = 0.13$).

Of participants with moderate malnutrition, 32.1% had a diagnosis of ESRD secondary to diabetes mellius compared to 14.6% of well-nourished participants. There was a significant association between moderate malnutrition and a diagnosis of ESRD secondary to diabetes mellitus ($p = 0.03$). Nearly fifty-six per cent (55.5%) of the participants had an albumin of ≥ 40 g/L. An albumin of < 40 g/L was significantly associated with moderate malnutrition (OR 3.68, $p = 0.001$). Pre-dialysis serum creatinine of < 880 μmol/L and total cholesterol of < 3.9 mmol/L were both significantly associated with moderate malnutrition, $p = 0.02$ and 0.04, respectively. A urea reduction ratio (URR) of < 65% was not significantly associated with malnutrition, $p = 0.15$.

One hundred and ten patients had hsCRP testing done. The mean hsCRP was 17.1 mg/L (0.3–275.5); 24.5% of those tested had hsCRP levels ≥ 10 mg/L and moderate malnutrition. Highly sensitive complement reactive protein levels of ≥ 10 mg/L were not significantly associated with moderate malnutrition, $p = 0.39$.

DISCUSSION

The male to female ratio in this study was 1.2:1 which is similar to the male:female ratio reported by Soyibo and Barton for Jamaica in the Report of the Caribbean Renal Registry, 2006 (21). The most common causes of renal failure in this study were diabetes, hypertension and chronic glomerulonephritis and which were also found in this report. However, the percentages of diabetes and hypertension were similar to that reported for Trinidad and Tobago and Bahamas than to those reported for Jamaica (21, 22). This difference could have been caused by more persons being diagnosed with diabetes in Jamaica over time and/or more patients with

a diagnosis of renal failure due to chronic glomerulonephritis rather than hypertension in this study. Since the first published data of the Caribbean Renal Registry, there has been an on-going campaign to improve diagnosis and identify the causes of CKD/ESRD in Jamaica and the Caribbean. Almost 50% of the participants were on dialysis for one to five years, while one-fifth of the study population was on dialysis for more than five years.

Slightly less than 50% of the study population had an AV fistula with only 14.5% of those on dialysis for up to six months having a fistula. The low percentage of persons initiated on haemodialysis with AV fistula could reflect the late presentation of patients with CKD. This implies that patients are presenting in later stages of CKD requiring dialysis without having enough evaluation and pre-dialysis work-up. This indicates that more emphasis and resources need to be placed on early diagnosis of CKD, allowing for proper evaluation and counselling pre-dialysis. There is increased risk of morbidity and mortality in patients who develop catheter sepsis and thrombosis with central venous catheters. How-ever, the overall percentage represents an improvement in the availability of AV fistula in Jamaica compared to data in 2006. Presence of an AV fistula was significantly associated with moderate malnutrition, $p = 0.01$. There has been correlation between AV fistula failure with malnutrition and infections. However, what is observed in this study could be due to late presentation of patients who already have malnutrition and thus had AV fistula after being on dialysis *via* central catheter. The presence of a permanent internal jugular catheter was associated with malnutrition ($p = 0.05$). There are correlating data suggesting the presence of catheter and malnutrition. This is related to increased risk of infection and increased level of inflammatory substance, putting the body in a catabolic state.

In the study population, 46.4% were overweight or obese. This is similar to percentages found in Western countries; however, this can represent sarcopenic obesity where there is loss of muscle mass and despite this, an excess of adipose tissue. This is seen in disease states where lack of physical activity leads to loss of muscle mass and gain in adipose mass. More than 75% of the study population had malnutrition and this is similar to percentages reported. Depending on the method used to evaluate malnutrition, 40–70% of ESRD patients are malnourished (23). Thirty-four per cent (34.5%) of persons with a BMI of ≥ 25 had malnutrition in this study.

End-stage renal disease due to diabetes mellitus was significantly associated with malnutrition. Diabetes with autonomic neuropathy causing gastroparesis results in vomiting, malabsorption and reduced caloric intake. The old adage "if the gut works, use it" may not necessarily help with the population of diabetics with this microvascular complication. Alternative mode of nutritional supplementation may be required. Intradialytic parenteral nutrition and other supplementation have been shown to be effective (24).

Participants on dialysis for up to six months had a significant association with being moderately malnourished. This is related to the high prevalence of malnutrition in patients with chronic renal failure who would later develop ESRD.

More than 50% of the participants had an albumin of ≥ 40 g/L. This was similar to that found in the Report of the Caribbean Renal Registry, 2006 (21). Albumin < 40 g/L was significantly associated with malnutrition and is found to be related to poor clinical outcomes and mortality in other studies (USRDS database/DOPPS).

A serum creatinine of < 880 μmol/L was significantly associated with moderate malnutrition in this study and is a marker of muscle wasting and is a risk factor for mortality according to the NKF/KDOQI Clinical Practice Guidelines for Nutrition in Renal failure (4).

A urea reduction ratio (URR) of < 0.65, corresponding to *kt/V* of 1.2, was not significantly associated with malnutrition. This has been reported in another study (24). It has been reported in patients with appropriate dialysis adequacy (*kt/V* > 1.2) that low serum albumin and low protein intake were associated with increased risk of hospitalization and mortality (22). However, neither the URR nor the *kt/V* has unambiguously predicted survival in haemodialysis patients. The ratio *kt/V* can be high because of either high *kt* or low *V*. Urea volume of distribution, V, may be a proxy for muscle mass/nutritional status. The equivocal relationship between URR or a *kt/V* and malnutrition is likely because malnutrition is multifactorial and reducing uraemia alone will not improve malnutrition. Looking at this in a different way, protein-calorie malnutrition will affect URR or *kt/V* thereby limiting its use as a marker.

Only 110 participants had hsCRP testing due to the relatively high cost of this test. Approximately 25% of those tested had an hsCRP of ≥ 10 mg/L and moderate malnutrition but this was not significant. A larger sample size may be significant. However, the cost of this test at this time may preclude it from being used as a regular marker of malnutrition in developing countries.

CONCLUSIONS

Factors associated with malnutrition in patients on dialysis were ESRD secondary to diabetes mellitus, dialysis duration for ≤ six months, low serum albumin, reduced pre-dialysis serum creatinine, low total cholesterol and presence of an AV fistula access. Therefore these factors should be assessed at the initiation of dialysis and protein energy malnutrition should be avoided in maintenance dialysis because of associated poor patient outcome.

Various forms of nutritional intervention may be needed for haemodialysis patients with malnutrition, including educating on nutrient-dense foods, supplemental oral feeds, enteral feeds through percutaneous gastrosotomy (PEG) tube, intradialytic parenteral nutrition and total parenteral nutrition (23, 24).

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