NUTRITIONAL ASSESSMENT OF STAGE 5 CHRONIC KIDNEY DISEASE PATIENTS ON HEMODIALYSIS

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BY

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INTRODUCTION:

Before 1970, therapeutic options for patients with kidney failure were quite limited. Only a small number of patients received regular dialysis because few dialysis facilities had been established. Patients underwent extensive medical screening to determine their eligibility for ongoing therapy, and treatment was offered only to patients who had renal failure as the predominant clinical management issue, (Bolton , 2003),(USRDS, 2003).

Patients with other systemic illnesses apart from kidney failure were not considered for chronic dialysis therapy. Kidney transplantation was in the early stages of development available as therapeutic option. Transplant immunology and immunosuppressive therapy were in their infancy, and for most patients, a diagnosis of chronic renal failure was a death sentence (Hariharan et al., 2000).

In the decade that followed, the availability of care for patients with kidney failure grew rapidly throughout the medically developed world. In the United States, the passage of Medicare entitlement legislation, in 1972, to pay for maintenance dialysis and renal transplantation, provided the major stimulus for this expansion. This trend continues unabated, at least for hemodialysis (Levey et al, 2002).

The gradual decline in kidney function in patients with chronic kidney disease (CKD) is initially asymptomatic. However, different signs and symptoms may be observed with advanced renal dysfunction, including volume overload, hyperkalemia, metabolic acidosis, hypertension, anemia, and bone diseases. The onset of end-stage renal disease results in a constellation of signs and symptoms referred to as uremia.

Manifestations of the uremic state include anorexia, nausea, vomiting, pericarditis, peripheral neuropathy, and central nervous system abnormalities (ranging from loss of concentration and lethargy to seizures, coma, and death). No direct correlation exists between the absolute serum levels of blood urea nitrogen (BUN) or creatinine, and the development of these symptoms. Patients may have relatively low levels (eg, a BUN of 60 mg/dL [21.4 mmol/L] in an older patient) but are markedly symptomatic; while others may have marked elevations (eg, a BUN of 140 mg/dL [50 mmol/L]) but remain asymptomatic.

To continue life, uremic patients require the institution of renal replacement therapy with hemodialysis, peritoneal dialysis, or renal transplantation. (Sarnak, MJ, et al. 2005), (Eriksen, ET al.2006), (Hallan, et al. 2006).

Despite numerous medical and technical advances, patients with kidney failure who are treated with dialysis often had constitutional symptoms as fatigue and malaise despite better management of anemia with erythropoietin. Progressive cardiovascular disease (CVD), peripheral and autonomic neuropathy, bone disease, and sexual dysfunction are common, even in patients who are considered to be treated adequately with dialysis.

Rehabilitation, particularly vocational rehabilitation, remains poor. Such findings are not unexpected, however, because the most efficient hemodialysis regimens currently provide only 10% to 12% of the small-solutes removal of two normally functioning kidneys. Removal of higher-molecular-weight solutes is even less efficient, (Lysaght MJ, 2002).

For most patients with kidney failure, kidney transplantation has the greatest potential for restoring a healthy, productive life. Kidney transplantation is the treatment of choice for end-stage renal disease. A successful kidney transplant improves the quality of life and reduces the mortality risk for most patients, when compared with maintenance dialysis, **(Vogt et al, 2007*).***

DEFINITIONS AND CLASSIFICATIONS:

The KDIGO 2012(Kidney Disease: Improving Global Outcomes) defined Chronic Kidney Diseases (CKD) in adults as abnormalities of kidney structure or function, present for>3 months, with implications for Health.

Criteria for CKD (either of the following present for >3 months)

Markers of kidney damage (one or more)	Albuminuria (AER >30 mg/24 hours; ACR >30 mg/g,>3 mg/mmol]
	Urine sediment abnormalities
	Electrolyte and other abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
Decreased GFR	GFR <60 ml/min/1.73 m2 (GFR categories G3a–G5)

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate. AER, albumin excretion rate; ACR, albumin-to-creatinine ratio.

STAGING OF CKD:-

--It is recommended that CKD is classified based on cause, GFR category, and albuminuria category (CGA).

-Cause of CKD is assigned based on presence or absence of systemic disease and the location within the kidney of observed or presumed pathologic-anatomic findings.

- GFR categorized into 5 stages which are assigned as follows:

Table 1

GFR categories in CKD

GFR category	GFR (ml/min/1.73 m2)	Terms
G1	>90	Normal or high
G2	60–89	mildly decreased*
G3a	45-59	mildly to moderately decreased
G3b	30–44	moderately to severely decreased
G4	15–29	severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.
*Relative to young adult level
In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Albuminuria* categorized into three stages which are assigned as follows

Table 2

Albuminuria categories in CKD

Category	AER (mg/24 hours)	ACR (approximate equivalent) (mg/mmol)	(mg/g)	Terms
A1	**<30**	**<3**	**<30**	**Normal to mildly increased**
A2	**30-300**	**3-30**	**30-300**	**Moderately increased***
A3	**>300**	**>30**	**>300**	**Severely increased****

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.
*Relative to young adult level.
Including nephrotic syndrome, (KDIGO 2012)**

*Where albuminuria measurement is not available, urine reagent strip results can be substituted

The purpose of this classification is to permit more accurate assessments of the frequency and severity of CKD in the general population, enabling more effective targeting of treatment recommendations.

Classification is based on estimated values for glomerular filtration rate (GFR) and the terms kidney failure or end-stage renal disease (ESRD) are used for patients with values less than 15 mL per minute,(KDIGO2012).

GLOMERULAR FILTRATION RATE:

Normal GFR — the glomerular filtration rate (GFR) is equal to the sum of the filtration rates in all of the functioning nephrons; thus, the GFR gives a rough measure of the number of functioning nephrons. The filtering units of the kidney, the glomeruli, filter approximately 180 liters per day (125 mL/min) of plasma. The normal value for GFR depends on age, sex, and body size, and is approximately 130 and 120 mL/min/1.73 m^2 for men and women, respectively, with considerable variation even among normal individuals, **(Stevens LA et al, 2006).**

Measurement of GFR:

The gold standard of exogenous filtration markers is inulin. Inulin is a physiologically inert substance that is freely filtered at the glomerulus, and is neither secreted, reabsorbed, synthesized, nor metabolized by the kidney.

Thus, the amount of inulin filtered at the glomerulus is equal to the amount excreted in the urine, which can be measured. Inulin, however, is in short supply, expensive, and difficult to assay. Furthermore, the classic protocol for measuring inulin clearance requires a continuous intravenous infusion, multiple blood samples, and bladder catheterization.

Various less cumbersome methods for measuring clearance are available: using alternative filtration markers (such as radioactive or nonradioactive iothalamate, iohexol , DTPA, or EDTA), bolus administration of the marker (subcutaneous or intravenous), spontaneous bladder emptying, and plasma clearance .While these methods are simpler, all have disadvantages that limit their application in clinical practice and affect the interpretation of research studies,(**Stevens LA,et al 2009).**

Estimation Equations:

GFR estimating equations improve upon the serum creatinine by incorporating known demographic and clinical variables as observed surrogates for the

unmeasured physiological factors other than GFR that affect the serum creatinine concentration, such as generation and tubular secretion. Estimation equations also appear to be reasonably accurate for following changes in GFR over time.

Similar to the serum creatinine, these equations do **not** provide accurate estimates of GFR in settings where the GFR is changing rapidly (eg, acute kidney injury). **(Wang X et al, 2006).**

The most common equations used in the United States are the Cockcroft-Gault and the MDRD study equations. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is more accurate than the MDRD study equation. The MDRD and CKD-EPI equations are normalized to body surface area.

Cockcroft-Gault equation:

The Cockcroft-Gault equation allows the creatinine clearance to be estimated from the serum creatinine in a patient with a stable serum creatinine

$$\text{CCr (mL/min)} = \frac{(140 - \text{Age}) \times \text{lean body weight [kg]}}{\text{Cr [mg/dL]} \times 72}$$

This formula takes into account assumptions that creatinine production decreases with advancing age, and is greater in individuals with greater weight. However, this equation was developed at a point in history when obesity was far less common. In the current era, higher weight may mean greater fat mass and not greater muscle mass. For Women, the formula requires multiplication by 0.85 to account for smaller muscle mass compared with men.The equation is not adjusted for body surface area. Therefore, to compare with normal values, the result should be adjusted for body surface area. Normalization for body surface increases the accuracy of this equation, particularly among those with decreased renal function**,** **(Shoker A, et al 2006).**

MDRD: (Modification of Diet in Renal Disease):

The MDRD study equation has been re-expressed for use with creatinine values that are standardized to creatinine reference materials measured using gold standard techniques. Standardized creatinine assays are used by most clinical laboratories in the United States.

GFR, in mL/min per 1.73 m^2 = 175 x SCr (exp [-1.154]) xAge (exp [-0.203]) x (0.742 if female) x (1.21 if black), where exp is the exponential.

(Levy AS et al, 2006).

CKD-EPI equation (The Chronic Kidney Disease Epidemiology Collaboration:

Both the MDRD study and the Cockcroft-Gault equations are less accurate in populations with normal or near normal GFR.

CKD-EPI is superior when GFR is normal or mildly reduced. The CKD-EPI equation was developed to provide a more accurate estimate of GFR among individuals with normal or only mildly reduced GFR (ie, above 60 mL/min per 1.73 m^2). This equation was developed using data pooled from 10 studies and validated against data derived from 16 additional studies, in which the gold standard was direct measurement of GFR using external filtration markers (eg, iothalamate). The study population included people with and without kidney disease who had a wide range of GFRs, **(Levey AS et al 2009).**

Prevalence of ESRD*:*

Chronic kidney disease is now recognized to be a worldwide problem associated with significant morbidity and mortality and there is a steep increase in the number of patients reaching end-stage renal disease. In many parts of the world, the disease affects younger people without diabetes or hypertension, **(Radhakrishnan et al 2014).**

Factors that may contribute to the greater increase in the prevalence of ESRD compared to CKD include improved survival from non-renal diseases and relaxed criteria for entry into ESRD programs, (Collins et al., 2010).

There are striking racial and ethnic differences in the incidence and prevalence rates of ESRD. In 2005, the incidence rates for ESRD in the United States were 268 per million populations in Caucasians, 991 in African Americans, 355 in Asian Americans and native Hawaiians and other Pacific Islanders, and 516 in American Indians and Alaska Natives, (Peralta et al., 2006).

Young blacks receiving dialysis have an increased risk of death compared with whites in the United States. Factors influencing this disparity among the young adult dialysis population have not been well explored, **(Johns TS, et al. 2014).**

Similarly, the incidence of ESRD in South Asian and African Caribbean immigrants in the United Kingdom is three to fourfold higher than in the

general population (Feehally et al, 2005). In 2012 the incidence rate in the UK was stable at 108 per million population (pmp) reflecting renal replacement therapy (RRT) initiation for 6,891 new patients, **(briggs V et al, UK renal registry 2012).**

Genetic factors underlie, at least in part, the markedly increased risk of ESRD among African Americans. These include Polymorphisms in genes that encode podocyte nonmuscle myosin IIA (MYH9) and apolipoprotein L1 (APOL1), (Palmer ND, et al 2014).

These genetic variations appear to confer a markedly increased risk for nondiabetic (Genovese et al., 2010) and diabetic (Freedman el al, 2009) ESRD.

<u>Scope of the problem in Egypt:</u>

Kidney disease is a growing problem .Prevalence of dialysis patients have increased from 10/million population in 1974 to 225/million population in 1996 (barsoum et al,1996).Recent data presented in the (3figure 1) points to an increasing trend accounting for 483/million population in 2004,(ESNT2004). A possible explanation is improved medical care for patients with chronic renal disease has contributed to annual increase in the numbers of patients who survive with End Stage Renal Disease.

A study done by Gouda Z, 2009 shows participants with evidence of CKD (e GFR<60 ml/min/1.73m2)were 4.7%, 71.9% were females and 37.5%with age >60 years. The modifiable risk factor of these participants was DM (12.5%), HTN (62.5%), Obesity (90.3%), and Smoking in males (22.2%) and Anemia (32.3%).There was limited awareness of the participants by the magnitude of CKD since only 29%of them were known to have CKD, (Gouda Z, 2009).

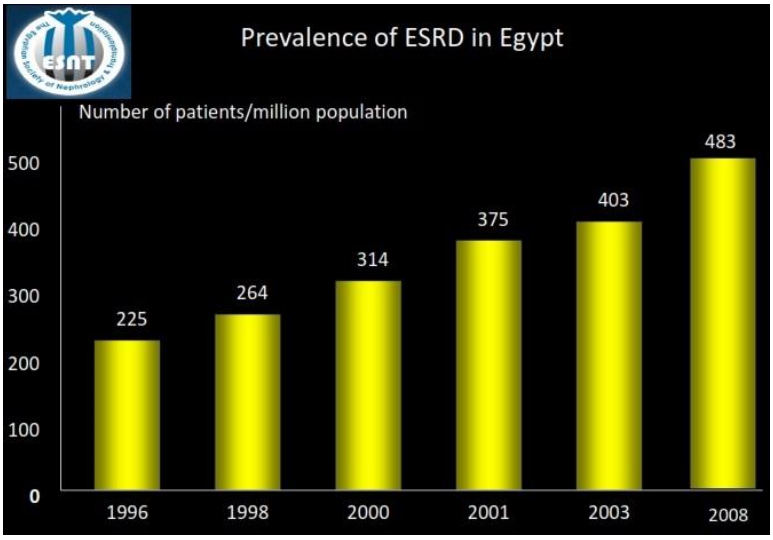

Figure 1

Therapeutic modalities for End stage renal disease

1) Hemodialysis

Hemodialysis is the predominant technique for treating ESRD throughout the world.

More than 485,000 Americans are being treated for end stage renal disease. Of these, more than 341,000 are dialysis patients and more than 140,000 have a functioning kidney transplant. Over the last five years, the number of new patients with kidney failure has averaged more than 90,000 annually**, (Zhang et al 2008, National Kidney Foundation, 2008).**

Chronic kidney disease is at least 3-4 times more frequent in Africa than in developed countries. Hypertension affects approximately 25% of the adult population and is the cause of chronic kidney failure in 21% of patients on renal replacement therapy in the South African Registry. The prevalence of diabetic nephropathy is estimated to be 14%-16% in South Africa, 23.8% in Zambia, 12.4% in Egypt, 9% in Sudan, and 6.1% in Ethiopia **,(National Kidney Foundation, 2009).**

In Egypt the prevalence rate of ESRD patients is presumed to have increased from 10 patients per million populations (PMP) in 1974 to about 300 patients PMP in 2001, **(Barsoum, 2002). Afifi, (2006)** stated that the prevalence of renal failure in Egypt is (483) patients PMP most patients are undergoing intermittent hemodialysis in governmental dialysis centers.

For highly motivated patients with a suitable living environment and a willing assistant, usually a spouse, hemodialysis can be done at home, the proportion of patients using home dialysis in Australia varies from 6% to 62% between renal units **(Fortnum, et al 2014).**

Home hemodialysis (HHD) is undergoing a significant revival. There is a global demographic shift with a rising mean age of dialysis patients**.** Cornelis T confirm in his study feasibility of HHD in patients 65 years or older at the start of this modality and should foster further research on the potential benefits of (intensive) HHD in older ESRD patients, (**Cornelis T et al, 2014**).

Hemodialysis is generally well tolerated, although ultrafiltration can cause hypotension, nausea, and muscle cramps. Older patients and those with established CVD may tolerate the procedure less well, (Stefanidis I 2002).

Over only a few hours, the intermittent nature of hemodialysis, which results in rapid changes in extracellular fluid volume, blood solute concentrations, and plasma osmolality, may contribute to fatigue and malaise after treatment. Concerns regarding dialysis efficiency and adequacy have received considerable attention in the nephrology literature in recent years, particularly with respect to their impact on patient morbidity and mortality. In addition, favorable outcomes in several small studies using alternative dialysis regimens, such as nightly, nocturnal hemodialysis or short-duration hemodialysis six times per week, serve to underscore the potential benefits of greater treatment duration and cumulative weekly solute removal on various clinical outcomes.

The decline in annual mortality in the U.S. ESRD population in recent years corresponds temporally with educational efforts to raise clinician awareness about the need for more efficient weekly dialysis prescriptions and with the more widespread use of objective measures of dialysis efficiency to monitor ongoing therapy. The K/DOQI guidelines published and updated by the National Kidney Foundation are an invaluable resource for the management of patients with CKD, (Lysaght et al., 2002),(Periera et al., 2002),(USRDS, 2003).

Vascular access failure from repeated cannulation procedures and the need for intermittent heparinization to prevent clotting in the extracorporeal blood circuit are additional concerns, particularly in diabetic patients (Ganesh et al., 2003).

Vascular access (VA) has a key role for successful treatment. Despite the advances that have taken place in the field of the HD procedure, few things have changed with regards to VA in recent years. Arteriovenous fistula (AVF), polytetrafluoroethylene graft and the cuffed double lumen silicone catheter are the most common used for VA. In the long term, a number of complications may present and more than one VA is needed during the HD life. The most common complications for all of VA types are thrombosis, bleeding and infection, the most common cause of morbidity in these patients. It has been estimated that VA dysfunction is responsible for 20% of all hospitalizations. A good functional access is also vital in order to deliver adequate HD therapy. It seems that the native AVF that Brescia and Cimino described in 1966 still remains the first choice for VA. The native forearm AVFs have the longest survival and require the fewest interventions. For this reason, the forearm AVF is the first choice, followed by the upper-arm AVF, the arteriovenous graft and the cuffed central venous catheter is the final choice**, (Pantelias K, et al 2012).**

2) Peritoneal Dialysis

Peritoneal dialysis was first used for the management of end-stage renal disease in 1959.-In 1968, Henry Tenckhoff developed the indwelling peritoneal catheter, which was placed via an open surgical technique-subsequently, percutaneous and laparoscopic techniques for placement have been utilized**, (Blagg CR, et al 2007). Peritoneal dialysis can be done either as Continuous ambulatory peritoneal dialysis (CAPD) or as Continuous cycling peritoneal dialysis (CCPD), (Teitelbaum I and Burkart J 2003)**.

Not only adequate uremic toxin removal but also volume control is essential in peritoneal dialysis (PD) to improve patient outcome, **(Fischbach, et al 2014). Peritoneal dialysis has certain advantages over hemodialysis, including the maintenance of relatively constant blood or serum levels of urea nitrogen, creatinine, sodium, and potassium. Hematocrit levels are often higher than for patients receiving hemodialysis, and gradual and continuous ultrafiltration may provide better blood pressure control. Because it is a form of self-care, peritoneal dialysis promotes patient independence (Lysaght, 2002).**