Suda0n University of Science and Technology

College of Graduate studies

Assessment of Nutritional Status Among Sudanese Patient Under Regular Hemodialysis

تقييم مستوى التغذية لدى المرضى السودانيين تحت الاستصفاء الدموي المنتظم

A dissertation submitted for partial fulfillment for the requirement of M. Sc degree in Medical Laboratory Science – Clinical Chemistry

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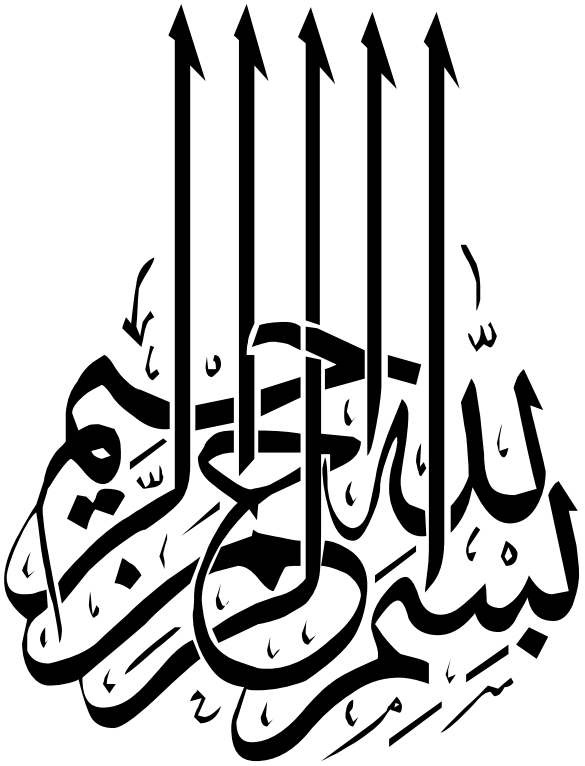
بسم الله الرحمن الرحيم

الآية

قال الله تعالى: (يَاأَيُّهَا الَّذِينَ آمَنُوا إِذَا قِيلَ لَكُمْ تَفَسَّحُوا فِي الْمَجَالِسِ فَافْسَحُوا يَفْسَحْ اللَّهُ لَكُمْ وَإِذَا قِيلَ انشُزُوا فَانشُزُوا يَرْفَعْ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ)

صدق الله العظيم

(المجادلة/11)

Dedication

To my husband

To my beloved family

To the soul of my mother

To my father

To my friends and teachers

Acknowledgement

First, I would like to express my gratitude to Allah for providing me the blessing to complete this work. I also would like to ask him that this project would be another tool to help dialysis patients. I am heartily thankful to my supervisor, Dr Abdelkariem Abubaker, whose encouragement, guidance, and support from the initial to the final levels enabled me to develop an understanding of the subject. Lastly, r offer my regards and blessing to all of those who supported me in any level during these thesis.

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Abstract:

Background:

Malnutrition is one of the complication among Sudanese patients under regular hemodialysis.

Objective:

To assess nutritional status of end stage renal disease patients under regular hemodialysis.

Material and Methods:

A cross-sectional study was conducted at different dialysis centers during the period from July to December 2016, the samples of 50 end stages renal disease out patient under regular dialysis and 50 samples included as control BMI was calculated in addition to serum Cholesterol and serum Albumin. Data was analyzed using statistical packages for social science (SPSS).

Results:

The majority of the patient in the age group (18-80) years on dialysis more than two years. All of them under went three sessions of hemodialysis per week

The mean value of BMI was (20.66 ± 2.87) and it is significant decreased (P=0.000).

The mean level of total Cholesterol of patient was significant elevated (162.12 ± 30.49) mg/dl compared to control (143 ± 38.88), P value= 0.015, while S.Albumin was decreased in cases compared to control, P value was (0.000) correlation studies.

Conclusion:

Low serum Albumin and BMI was observed in patients under hemodialysis which is indicated of malnutrition.

مستخلص البحث

يعتبر سوء التغذية احد المضاعفات المصاحبة للمرضي السودانيين ذوي الاستصفاء (الغسيل) الدموي المنتظم.

الهدف:

تقييم الحالة الغذائية لمرض المرحلة النهائية من امراض الكلى ذوي الاستصفاء الدموي المنتظم.

المواد والطرق:

في دراسة مستعرضة اجريت من مختلف الاستصفاء في الفترة مابين يوليو الي ديسمبر شملت 50 عينة دموية لمرض الفشل الكلوي ،تم حاب مؤشر كتلة الجسم بالاضافة الي قياس تركيز الكلوسترول والالبيومين في مصل الدم، كما اتم تحليل البيانات باستخدام الحزمة الإحصائية للعلوم الاجتماعية .

النتائج:

اغلبية المرضي تتراوح اعمارهم مابين(18–80) عاما جميعهم خضعون للغسيل الكلوي لمايزيد عن العامين بمعدل ثلاث مرات اسبوعياً.

متوسط قيمة موشر كتلة الجسم هو (2.87–20.66) مع قيمة احتمالية (0.00)

سجل تركيز كولسترول الدم للمرضى ارتفاعا (36.49–162.12)مجم /دلتر مقارنة بتركيزه لدي فئه الاصحاء (38.33–143.44)مجم/ دلتر عند القيمة الاحتمالية (0.015)بينما كان تركيز الالبيومين منخفضاً للمرضي (33.3 ± 0.51) مقارنة بذات الفئة السليمة (4.22 ± 0.60)عند القيمة الاحتمالية (0.00).

ايضاً يوجد تناسبا عكسيا بين مستوى الالبيومين في الدم (جم/دلتر) والفترة الزمنية للغسيل الكلوي (بالسنوات) عند القيمة الاحتمالية (0.026) ومعامل التصحيح (−0.31) بينما كان هناك تناسبا طرديا بين مستوى كولسترول الدم (مجم/دلتر) وذات الفترة الزمنية (بالسنوات) عند معامل التصحيح (0.015) والقيمة الاحتمالية (0.920).

الخلاصة :

سجل مستوي الالبيومين في الدم ومؤشر كتلة الجسم لدي مرضي الغسيل الكلوي المنتظم انخفاضاً مما يشير الي وجود سوء في التغذية.

Chapter One
Introduction and Literature Review

1. Introduction

The kidneys filter waste and excess water from the blood as urine. Chronic kidney disease (CKD), caused kidneys to lose this function over time. End-stage kidney disease (ESRD) is the final stage of chronic kidney disease. It means that kidneys no longer function well enough to meet the needs of daily life and it can be below 10 percent of their normal ability, which may mean they are barely functioning or not functioning at all .(Christine Dl Maria. 2016). End stage of renal disease (ESRD) is one of the problem all over the world, currently, hemodialysis represent the main mode for treatment of chronic kidney disease stage 5(CDK5). (Shalabia et al, 2015). Complications of end stage of renal disease (ESRD) include drug toxicity, metabolic and endocrine complications, and increased risk for CYD. It occurs at any stage and associated with co-morbidity if not treated. (Andrew S. et al., 2005) Treatment of progression in renal function normally occurs in the most developed stages of the disease (stage 5) requiring either dialysis or transplant Treatments available in terminal renal diseases are: Continuous Ambulatory Peritoneal Dialysis (CAPD), Automated Peritoneal Dialysis (APD), Intermittent Peritoneal Dialysis (IPD), Hemodialysis (HD), and renal transplant. Hemodialysis is a procedure that depends on a dialyzer (capillary filter) to filter the blood. In the procedure, patients' blood is withdrawn from one vein, through an arteriovenous fistula or a catheter and taken directly by tubes to a filter connected to a machine. (Benzerra and Santos J., 2008). During recent years, several studies in HD patients have shown an association between signs of malnutrition, particularly low serum albumin, and increased morbidity and mortality. However, the extent to which this reflects a cause-effect relation-ship is not clear, since several co-morbidity factors, which are of more importance as causes of death, may have secondary effects on various parameters used to assess

the nutritional status (Qureshi et al., 1998). Hemodialysis modality seems to be more advantageous for malnutrition components than peritoneal dialysis, but large proportions of patient demonstrate sign of protein-energy malnutririon which can detected by estimate serum protein and total serum cholesterol. (Tonbul et al, 2006). The presence of protein-energy malnutrition (PEM) is one of morbidity and mortality in end stage of renal disease (ESRD), patients receiving maintenance hem dialysis (HD) therapy Ishalabia et al, 2015). Malnutrition is considered markers of poor prognosis In CKD, several studies suggest that the prevalence of malnutrition in HOP varies dramatically across the world ranging from under 10% to over 90%. The patients nutritional status is inversely associated with increased risk of hospitalization and mortality thus constituting an important risk factor for the outcome of these patients. (shalabia et al, 2015).

1-2 literature review:

1-2 -1 location of kidneys:

Kidneys are a pair of bean like shape organs located posterior to the abdomen and below the rib cage. Renal size and volume decrease with age, accompanied by intra renal vascular changes. The number of glomeruli decreases and the mass of the juxta medullary nephrons falls. The result is a decrease in the filtration area of the glomerular basement membrane and decreased permeability. The glomerular filtration rate (GFR) is reduced with aging. (Lurban M .,1995)

1-2-2 Functions of kidneys:

I-maintain H20 and salts balance in the body.

2-maintain proper Osmolarity of body's fluid, primarily through regulating H20 balance

3-regulate the quantity and concentration of most ECF ions.

4-maintain proper plasma volume.

5-help maintain proper acid - base balance in the body.

6-excreting (eliminating) the end products (wastes) of the body metabolism.

7- excreting many foreign compounds.

8- Producing erythropoietin and rennin

9- Converting vitamin D in to its active form. (v. cmpbll, 2010).

1-3 kidney disease:

1-3-1 Glomerulonephritis (nephritis)

It is an important cause of renal impairment accounting for 10%-15% of cases of end stage renal failure all over the world, following only diabetes and hypertension in importance. It is associated with a nephritic syndrome that is with haematuria, proteinuria, and impaired renal function together with hypertension, fluid overload, and oedema. Their pathology involves intra glomerular inflammation and cellular

proliferation with secondary renal impairment over days to week (Vinen C, Oliveira D.,2003)

1-3-2 Pyelonephritis:

Acute pyelonephritis is a common bacterial infection of the renal pelvis and kidney most often seen in young adult women. History and physical examination are the most useful tools for diagnosis. Most patients have fever, although it may be absent early in the illness. Flank pain is nearly universal, and its absence should raise suspicion of an alternative diagnosis. Escherichia coli is the most common pathogen in acute pyelonephritis, and III the past decade, there has been an increasing rate of E. coli resistance to extended-spectrum beta-lactam antibiotics (Richard C, Mozella W.,2011).

1-3-3 Kidney Stones (calculi):

Kidney stones affect up to 5% of the population, with a lifetime risk of passing a kidney stone of about 8-10%, Increased incidence of kidney stones in the industrialized world is associated with improved standards of living and is strongly associated with race or ethnicity and region of residence, Recent evidence indicates that formation of kidney stones is a result of a nonobacterial disease akin to Helicobacter pylori infection and peptic ulcer disease. Nanobacteria are small intracellular bacteria that form a calcium phosphate shell (an a patite nucleus) and are present in the central nidus of most (97%) kidney stones and in mineral plaques (Randall's plaques) in the renal papilla, Further crystallisation and growth of stone are influenced by endogenous and dietary factors. (Malvender.,2004)

1-3-4 Kidney Cancer:

Renal cell carcinoma (RCC), also known as renal cell cancer or renal cell adenocarcinoma, is by far the most common type of kidney cancer (RCC) usually grows as a single tumor within a kidney, sometimes there are two

or more tumors in one kidney or even tumors in both kidneys at the same time. There are several subtypes of RCC, based mainly on how the cancer cells look under a microscope. Knowing the subtype of RCC can be a factor in deciding treatment and can also help your doctor determine if your cancer might be due to an inherited genetic syndrome. Staging systems are designed to reflect the modes of spread and are used to stratify treatment options and to assess prognoses and survival characteristics.(Chaan et al., 2008)

1-3-5 Polycystic Kidney Disease

Polycystic kidney diseases are a leading cause of end-stage renal failure and a common indication for dialysis or renal transplantation. Recent advances have led 10 insights into mechanisms underlying the cause and prognosis of these diseases and suggest new directions for treatment. Polycystic kidney disease may arise sporadically as a developmental abnormality or may be acquired in adult life as a consequence of aging, but most forms are hereditary which are due to germ-line mutations in single genes, inherited as mendel ian traits, include autosomal dominant and autosomal recessive polycystic kidney disease, nephronophthisis, and medullary cystic diseases.(Patricia D.,2004)

1-3-6 Renal Infarction

Acute renal infarction is a rare cause of acute abdominal pain. It has to be expected in the patients with cardiovascular risk factors. Most accurate diagnostic tool is the helical CT scan of abdomen.(Sherif A et al.,20 14).

Once it is diagnosed, preferred therapies are percutaneous endovascular therapies, anticoagulation, or thrombolysis. If the diagnosis is missed, there is an increase in mortality and morbidity as a consequence of declining renal function or even failure. (Sherif A et a1.,2014).

1-3-7 Renal Vein clot:

The term renal vein thrombosis (RVT) or clot is used to describe presence of thrombus in the major renal veins or their tributaries. This condition may either present with acute symptoms or go unnoticed because of lack of symptoms until a complication like pulmonary embolism or worsening renal function, draws attention to it. This syndrome is responsible for a hyper coagulable state. The excessive urinary protein loss is associated with decreased antithrombin Ill, a relative excess of fibrinogen, and changes in other clotting factors; all lead to a propensity to clot. Numerous studies have demonstrated a direct relation between nephrotic syndrome and both arterial and venous thromboses.(Muhammed A et al 2007).

1-3-8 Acute kidney disease:

Which characterized by a rapid deterioration in kidney function manifested by an increase in serum creatinine level with or without reduced urine output. the diagnostic evaluation can be used to classify acute kidney injury as pre renal, intrinsic renal .or post renal .(Mahboob R., 2012). Acute kidney disease which increase the risk for chronic kidney disease and end stage of renal disease ESRD.(Mahboob .R., 2012)

1-3-9 Chronic kidney disease:

It is defined as an irreversible and progressive reduction in the glomerular filtration rate (GFR) to below 25% of normal level (decline of 30 ml/min/I.73m2) for at least three months. (Foreman J, Chan J ., 1988)

1-4 Stages of renal disease:

Different degrees of renal dysfunction from the earliest kidney damaged to ESRD have been classified into the following five stages on the basis of markers of kidney damage and level of kidney function (glomerular filtration rate GFR). End stage renal disease (ESRD) is characterized by failure of the kidneys to remove waste products and excess fluid from the

body. (NKF., 2002) Chronic kidney disease (CKD) is a progressive condition marked by deteriorating kidney function over time. Typically, kidney function is quantified by glomerular filtration rate (GFR), with (GFR) most frequently estimated using equations that incorporate serum creatinine along with demographic data. I The early stages of CKD (stages I and 2) are manifested by kidney damage and are generally asymptomatic; the kidney functions normally but the risk for progressive disease is significant. As kidney disease worsens, kidney function begins to deteriorate (stages 3 and 4 CKD). Eventually, kidney failure (stage 5 CKD) ensues and kidney replacement therapy is required.(Daniel E.,2007)

-Stage l: normal GFR>=90ml/min per l.73m2 and persistent albumin

-Stage 2: GFR between 60 to 89ml/min per 1.73m2

-Stage 3: GFR between 30 to 59 ml/min per 1.73m2

-Stage 4: GFR between 15 to 29 ml/min per 1.73m2

-Stage 5: GFR <of 15 ml/min per 1.73m2 which is end stage or renal failure (NKF,2002)

1-5 Renal failure 1-5-1 definition

Renal Failure known as inability of the KIDNEY to maintain normal function, so that waste products and metabolites accumulate in the blood. This affects most of the body's systems because of its important role in maintaining fluid balance, regulating the electrochemical composition of body fluids, providing constant protection against acid-base imbalance, and controlling blood pressure. Called also kidney failure. (Daniel E., 2007) .

1-5-2 Signs and symptoms

End stage renal disease is initially without specific symptoms and is generally only detected as an increase in serum creatinine or protein in the urine. As the kidney function decreases (Bacchetta, et at. 2012).

-Blood pressure is increased due to f1uid overload and production of vasoactive hormones created by the kidney via the renin-angiotensin system, increasing one's risk of developing hypertension and/or suffering from congestive heart failure. (Bacchetta et al., 2012).

-Urea accumulates, leading to azotemia and ultimately uremia (symptoms ranging from lethargy to pericarditis and encephalopathy). Due to its high systemic circulation, urea is excreted in eccrine sweat at high concentrations and crystallizes on skin as the sweat evaporates. (Bacchetta, et al. 2012)

-Potassium accumulates in the blood (hyperkalemia with a range of symptoms including malaise and potentially fatal cardiac arrhythmias). Hyperkalemia usually does not develop until the glomerular filtration rate falls to less than 20-25 ml/min/l.73 m2, at which point the kidneys have decreased ability to excrete potassium. Hyperkalemia in CKD can be exacerbated by acidemia (which leads to extracellular shift of potassium) and from lack of insulin. (Bacchetta et al., 2012) -Fluid volume overload symptoms may range from mild edema to life-threatening pulmonary edema (Bacchetta et al., 2012).

- Hyper phosphatemia, due to reduced phosphate excretion, follows the decrease in glomerular filtration. Hyper phosphatemia IS associated with increased cardiovascular risk, being a direct stimulus to vascular calcification. (Bacchetta, et al. 2012)

- Hypocalcemia, due to 1, 25 dihydroxyvitamin D3 deficiency, is caused by stimulation of fibroblast growth factor-23. Osteocytes are responsible for the increased production of FGF23, which is a potent inhibitor of the enzyme I-alphahydroxylase (responsible for the conversion of 25 hydroxycholecalciferol into 1,25dihydroxyvitamin D3). Later, this progresses to secondary hyperparathyroidism, renal osteodystrophy, and

vascular calcification that further impair cardiac function (Bacchetta, et al. 2012).

- Metabolic acidosis (due to accumulation of sulfates, phosphates, uric acid etc.) may cause altered enzyme activity by excess acid acting on enzymes; and also increased excitability of cardiac and neuronal membranes by the promotion of hyperkalemia due to excess acid (acidemia). Acidosis is also due to decreased capacity to generate enough ammonia from the cells of the proximal tubule. (Bacchetta, et al. 2012)

-Iron deficiency anerma, which increases in prevalence as kidney function decreases, is especially prevalent in those requiring haemodialysis. It is multi factoral in cause, but includes increased inflammation, reduction in erythropoietin, and hyperuricemia leading to bone marrow suppression (Bacchetta, et al. 2012).

1-5-3 Treatment

1- Renal Replacement Therapy (RRT) include

Dialysis: It's a treatment that takes over kidney functions if those organs stop doing their job. There are two types of dialysis:

-**Hemodialysis** : the blood is put through a filter outside body, cleaned, and then returned to the body. This is done either at a dialysis facility or at home. (Rajnish.,2011).

-**Peritoneal dialysis**: the blood is cleaned inside the body. A special fluid is put into the abdomen to absorb waste from the blood that passes through small vessels in abdominal cavity. The fluid is then drained away. This type of dialysis is typically done at home (Rajnish 2011).

2-Kidney transplant: A surgical procedure USIng a donor kidney to treat renal failure. Transplantation is a preferred treatment over dialysis because of its improved outcome. (Rajnish 2011). The principal problems in kidney transplantation are immunologic, r.e. avoiding rejection of the transplanted kidney by the recipient's immune system (Rajnish ,2011)

1-6 Hemodialysis 1-6-1 Definition

Hemodialysis is the most common type of dialysis. It uses an artificial kidney, known as a hemodialyzer, to remove waste and chemicals from blood. To get the blood to flow to the artificial kidney, the doctor will surgically create a vascular access, or an entrance point, into the blood vessels. This vascular access will allow a larger amount of blood to flow through the body during hemodialysis treatment. This means more blood can be filtered and purified (Rajnish M.,20l1)

1-6-2 complications of hemodialysis

-Fluid imbalance

Because the kidneys are primarily responsible for the regulation of fluid and electrolyte balance, acute or chronic changes in renal function can result in multiple imbalances. Acutely, the rapidity of onset of renal deterioration makes nursing assessment and intervention critical to the prevention of complications and potentially fatal outcomes. For patients with chronic renal failure, nursing assessment and intervention are equally significant, since there is an absence of renal regulatory mechanisms. In renal failure, acute or chronic, one most commonly sees patients who have a tendency to develop hypervolemia, hyperkalemia, hyperphosphatemia, hypocalcemia, and bicarbonate deficiency (metabolic acidosis). Sodium is generally retained, but may appear normal, or hyponatremic, because of dilution from fluid retention. Following the relief of a urinary tract obstruction, hypovolemia;' hyponatremia (true loss of sodium), hypokalemia, hypocalcemia, hypomagnesemia, and bicarbonate loss are most apt to occur. Electrolyte imbalances after urinary diversion vary depending on the site of urine diversion. (Chamber J,1987)

-Hypertension

Hypertension is a well established cause, a common complication, and an important risk factor for progression of renal disease. Controlling hypertension is the most important intervention to slow the progression of renal disease. Any antihypertensive agents may be appropriate, but angiotensin converting enzyme inhibitors are particularly effective in slowing progression of renal insufficiency in Patients with and without diabetes by reducing the effects of angiotensin II on renal hemodynamic, local growth factors, and perhaps glomerular perm selectivity. Non-dihydropyridine calcium channel blockers have also been shown to retard progression of renal insufficiency in patients with type 2 diabetes. Recently, angiotensin receptor blockers (irbesartan and losartan) have been shown to have a renoprotective effect in diabetic nephropathy, independent of reduction in blood pressure. Early detection and effective treatment of hypertension to target levels is essential. The benefit of aggressive control of blood pressure is most pronounced in patients with urinary protein excretion of>3 g/24 hours. (Malvider S., 2002)

Hyperkalaemia.

This compliant may develop due to suppression of aldosterone-dependent colonic excretion of potassium by Angiotensin Converting Enzyme (ACE) inhibitors or to inhibition of post-prandial transport of potassium into cells by beta blockers. In ESRD patients, there is an adaptive Increase in potassium excretion by the gut. Nevertheless, this adaptation is insufficient to compensate for the loss of renal excretory capacity.

The two major physiologic factors that stimulate potassium disposal are insulin and epinephrine. (Michael A., 1995)

Renal Anemia

Renal anemia, which is often associated with fatigue and cognitive and sexual dis function, has a significant impact on the quality of life of

patients with CKF. Anemia has also been identified as an important etiologic factor in the development of left ventricular hypertrophy, an independent risk factor for heart failure and a predictor of mortality in HD patients (Golper et al., 2003). The major cause of renal anemia in CKF is an inadequate production of the glycoprotein hormone erythropoietin (EPO) because of a reduction in functional kidney parenchyma (Santoro ., 2002). Furthermore, free radicals elicited from leucocytes by their contact with the dialysis membrane cause hemolysis with consecutive anemia in CKF patients on extracorporeal renal replacement therapy (Eiseltet al., 1999)

Other vitamin deficiencies

Due to effect of dialysis process on normal absorption, retention and activity of necessary micronutrients which support all aspects of carbohydrate, protein, lipid and nucleic acid metabolism, renal failure patients require vitamin replacement therapy that addresses the specialized needs of renal failure. Studies have shown that the typical renal failure diet is low in B vitamins, that uremic factors affect folate and pyridoxine activities and that many B vitamins are lost on dialysis at a rate greater than are lost with normal urinary excretion. In addition, retention of vitamin A or inappropriately high supplementation of vitamin C may cause toxicities which exacerbate existing pathologies. Further, emerging research suggests some vitamins such as folic acid and pyridoxine, if provided in higher than normal amounts, may have an impact on reducing the risk of some aspects of renal cardiovascular disease. It is therefore important to supplement some vitamins, and use restraint in the supplementation of others. It is clear that renal failure patients, including predialysis, ESRD and transplant patients need specialized supplementation that meets the requirements of disease and its management. (Makoff R., 1999).

Bone and joint Disease:

Dialysis patients are at risk of osteomalacia (due to defective renal hydroxylation of vitamin D), hyperparathyroidism (due to phosphate retention, calcium malabsorption, and defective hydroxylation of vitamin D), and may also develop osteoporosis. These conditions may be a symptomatic in the early stages but may result in bone and joint pain or pathological fractures. Patients on long-term dialysis are prone to the development of stiffness and aching in the joints, particularly the shoulders. This is related to accumulation of amyloid deposits. Treatment is difficult, but the symptoms respond to successful renal transplantation. Low dose steroid treatment may be effective. Vascular and extra articular calcification. This is caused by hyper para thyroidism, phosphate retention, and positive calcium Balance. Phosphate retention is treated by dietary restriction and by administration of "phosphate binders". (Kevin J et aI., 2007) Cardiac Disease: Cardiovascular disease is responsible for much of the premature mortality of dialysis patients. This is nearly certainly due to the effects of longstanding anaemia, hypertension, and fluid overload on the myocardium, and to a high incidence of pre-existing atherosclerotic cardiovascular disease in patients presenting with renal failure. In addition, patients may develop calcification of the aortic and mitral valves associated with phosphate retention.(Richard S., 2015) Those who undergo long-term dialysis treatments are also at risk of developing other medical conditions, including amyloidosis. This disease can occur when amyloid proteins produced in bone marrow build up in the kidneys, liver, heart, and other organs. This usually causes joint pain, stiffness, and swelling. Some people may also develop depression after being diagnosed with long-term kidney failures. (Richard S.,2015).

Malnutrition:

During chronic renal failure, malnutrition is responsible for increased morbidity and mortality. Both protein and energy intakes decrease during the course of renal insufficiency. Abnormal nutrient metabolism, which concerns both protein and energy metabolism, in peripheral as well as in hepatosplanchnic tissues, contributes to the development of malnutrition. Before dialysis therapy is instituted, protein restriction is usually recommended. However the occurrence of malnutrition argues for the initiation of dialysis therapy and the increase of protein intake. During dialysis, severe malnutrition in found in 25% of patients and compromises the prognosis. Indicators of protein nutrition such as protein catabolic rate, serum albumin and prealburnin, which are the best markers of the prognosis, must be integrated in the follow-up of these patients. In dialysis patients, the estimated nutritional requirements are 35-40kcal et I.2-1.4g protein/kg/day. In malnourished dialysis patients, after verification of the adequacy of dialysis therapy, nutritional support should be chosen according to its ability to satisfy these nutritional needs, taking into account the spontaneous intakes(Cano N .,2000).

1-7 The pathogenesis of malnutrition in hemodialysis patient

There are two fundamentally different types of malnutrition in patients with chronic renal failure, the first is related to low protein and energy intake, which characterized by normal serum albumin or slightly decreased and co-morbid condition are un common. This type of malnutrition may be amenable to adequate nutritional and dialysis support. In contrast, the second type of malnutrition is associated with inflammation and atherosclerotic cardiovascular disease (MIA syndrome). Co-morbid conditions are common and serum albumin levels are usually decreased. This type of malnutrition is much more difficult to reverse with nutritional support and dialysis therapy, unless the

underlying co-morbid conditions and chronic inflammatory response are adequately treated. (Francesco L, et al., 2002). A low serum albumin level has been used as a marker for malnutrition and it can decrease in both inflammation and inadequate nutritional intake. On the other side, patients on maintenance dialysis may have elevated levels of pro - inflammatory cytokines, which lead to malnutrition by acting directly on the gastrointestinal system or indirectly through affecting appetite and resting energy expenditure or by mediating increased protein hydrolysis and muscle protein breakdown (Roberto., 2002). Patients may not ingest sufficient amounts of food because of loss of appetite. Anorexia can be caused by factors such as the retention of uraemic toxins and chronic metabolic acidosis, which, moreover, is an important catabolic factor. In this regard, inadequacy of dialysis treatment may be an important cause of malnutrition. Renal replacement therapy per se causes a loss of nutrients. During a haemodialysis (HD) session, a considerable quantity of amino acids may be lost (4-9 g in the fasting state). In contrast, protein losses are negligible, unless multiple re-use of dialysis filters is practised. Peritoneal dialysis (PD) causes a loss of peptides, 9 g of total protein and 6 g of albumin daily, and even much more during episodes of peritonitis. Both HD and PD can cause a loss of vitamins, particularly water-soluble vitamins. Endocrine and metabolic disturbances of uraemia, in particular insulin resistance, can reduce protein anabolism and favour catabolism. The role of psychological factors (depression) and socio-economic factors (loneliness, invalidity, poverty) should never be neglected, considering that at present the majority of the dialysis population is composed of elderly patients. Acute concurrent illnesses can also contribute .to malnutrition. Finally, inadequate dietary prescription, due to the traditional physician's preference of prescribing nutritional restriction

rather than providing nutritional counseling, can further worsen malnutrition. (Francesco L et al., 2002).

1-8 Dietary supplements

In patients where oral dietary intake from regular meals cannot maintain adequate nutritional status, nutritional supplementation, administered orally, eternally, or parent rally, is shown to be effective in replenishing protein and energy stores. In clinical practice, the advantages of oral nutritional supplements include proven efficacy, safety, and compliance. Anabolic strategies such as anabolic steroids, growth hormone, and exercise, in combination with nutritional supplementation vr alone, have been shown to improve protein stores and represent potential additional approaches for the treatment of PEM appetite stimulants, (Ikizler T A., 2013).

1-9 Prevalence and Magnitude of malnutrition among Chronic renal failure patients world wide:

A prospective cohort study done by(Sunna Snadel et al .,2015) comparing between effects of modalities of dialysis in nutritional and inflammation, their study concluded that Protein Energy Wasting (PEW) lead to increased inflammation and malnutrition's rate after correcting for age, sex, dialysis vintage, modality and co-morbidity in hemodialysis patients, and increased co-morbidity predicted IL-6, but not CRP. Also they found that Circulating concentrations as IL-6 and CRP levels were higher and protein, albumin and total lipid profile were low. Many previous studies (Koople JD .,1997 ;Qureshi AR et al .,1998 ; Araujo IC et al.,2006 ; Afshar R et al.,2007 ;Shegall et aI., 2008)have reported that there are several psychosocial and co-morbidity factors that may hamper adequate nutrition. There are also several factors in dialysis patients that may enhance protein catabolism and increase protein requirements, such as low energy intake, metabolic acidosis, dialectic loss of glucose, protein and amino acids and other catabolic effects of the dialectic procedures, as well as effects of infections and other comorbidity factors.

Study done by (Bellizzi. V et al.,2003) of nutrition intake in hemodialysis show that well-nourished haemodialysis patients, in absence of known risk factors for malnutrition, All patients showed a day-by-day reduction of whole nutrient intake during inter dialectic period, which was mostly relevant in the third inter dialectic day (L3). During the I-year study, even in the presence of adequate dialysis dose and normal inflammatory indexes, decreased body weight, and decreased serum albumin Diaries evidenced in low a reduced number of meals at L3 that was explained by the fear of excessive interdialectic weight gain. During the interventional study, daily protein and calorie intake DPI and DCI increased at L3; this was associated with a significant increment of body weight, and serum albumin and creatinine levels. They hypothesized that in maintenance haemodialysis patients the persistent, marked reduction of daily nutrient intake, even if limited to a single day of the week, is an independent determinant of reversible impairment of nutritional status. Another study done by (Bossola M et al .,2005) This study shows that dietary energy and protein intakes are inadequate in the majority of HD patients and are negatively related to the presence of anorexia and age. These data may be potentially useful in the identification of nutritional strategies as well as in improving food intake in HD patients. The study done by (T. Alp., 2013) it show that In patients with stage 3-5 CKD on maintenance dialysis, nutritional screening should include assessments of serum albumin, weight loss, and a malnutrition screening tool at every outpatient clinic visit. For that receiving in-center maintenance HD, this should be performed monthly. In patients deemed to be at risk for PEW, anthropometric measurements, subjective global assessment, or malnutrition-inflammation score should be performed every 6 months, in addition to periodic measurements of serum prealbumin, high-sensitivity C-reactive protein, and cholesterol. All agree in low albumin is one of the

markers of poor or malnutrition, also the age have a negatively correlation with energy intake. On the other hand, regular follow up of patient nutrition may decreased mortality and morbidity for them. The study done (AL Sarank et al .,2011) was performed to assess the nutritional status among patients on maintenance hemodialysis at the Prince Salman Center for kidney disease. Found that the patients weight average between under, normal, over and, morbid obesity. Severe malnutrition by body weight correlated with duration of dialysis, functional capacity, and associated co-morbid diseases. A study done by (Silbiger SR.,1995) explain the role of gender on the progression of chronic renal disease shown that the rate of progression of renal disease is influenced by gender. Deterioration of renal function in patients with chronic renal disease is more rapid in men than in women, independent of differences in blood pressure or serum cholesterol levels. In addition to genetically determined differences between the sexes in renal structure and function, sex hormones may directly influence many of the processes implicated in the pathogenesis of renal disease progression. Potential mechanisms include receptor-mediated effects of sex hormones on glomerular hemodynamic and mesangial cell proliferation and matrix accumulation as well as effects on the synthesis and release of cytokines, vasoactive agents, and growth factors. In addition, estrogens may exert potent antioxidant actions III the mesangial microenvironment, which may contribute to the protective effect of female gender.

1-10 The Rationale

Many studies all over the world have reported the presence of malnutrition in a large number of hemodialysis patients. The majority of these studies revealed that protein-energy wasting was associated morbidity and mortality, and impaired quality of life. Several markers, such as low body mass index (BMI)(weight/high 2), low S.albumin, low S.cholesterol and elevated C-reactive protein (CRP) have been associated with under nutrition in population of hemodialysis patient. In Sudan, many studies published that address the assessment of malnutrition in hemodialysis patients. All hypothesized that, most hemodialysis patient suffering from poor nutritional state and by increase time of duration, they will go worse, and must attention for them.

1-12 Objectives:

1-12-1 General objective:

To assess the nutritional status of Sudanese patients under regular hemodialysis by measuring serum albumin and serum cholesterol levels

1-12-2 Specific objective:

1. to determine S. albumin and S cholesterol in patient under regular h odialysis
2. to correlate between S. albumin - S .cholesterol and duration of hemodialysis
3. to correlate between S. albumin - S .cholesterol and BMI
4. to correlate between S. albumin -S. cholesterol and gender and age.

Chapter two
Materials and Methods

Material and method

2-1 Study area

This study was conducted from different dialysis units of Khartoum state.

2-2 Study design:

A descriptive core-control study conducted between July to December 2016.

2-3 Study population

Study done on patient with renal failure who was attended three times weekly to the hemodialysis dialysis unit.

2-4 Sample size

Fifty sample of regular hemodialysis who agree to participate in the study and were randomly selected (25) male, (25) female, and 50 control of healthy people.

2-5 Inclusion criteria

Samples were collected from patients were 3 time attended to hemodialysis unit at the hospital.

2-6 Exclusion criteria

Subject with minimum stress, were affect on albumin result.

Subject who suffering from fatigue and have a bad psychological state.

Subject who breaking fast, were affect on cholesterol result.

2-7 Collection of samples:

One hundred (100) blood samples was collected by sterile syringes in Heparin containers, then centrifugated at 4000 RPM immediately before transferred to plain containers, and plasma stored.

2-8 Ethical Consideration:

Explaining the purpose of the study and assuring the confidentiality of all participants, a verbal informed consent was obtained from each participant.

An approval for the study was granted from ethical committee of Sudan university of science and technology, before starting the subject's recruitment process. The approval was obtained from the administrators of the selected hospitals. A cover letter that explains the purpose of the study.

2-9 Method of S. Albumin (Bromo Cresol Green BCG):

0.01 ml of sample added to 1 ml from BCG reagent ,mix and wait for One min ,then read against blank at 630 nm.

2-10 Principle of BCG

Albumin in the sample reacts with bromocresol green in acidic media forming a colour complex that can be measured by spectrophotometry

2-11 Method of S. cholesterol (CHOD/PAP);

0.01ml of serum added to 1 ml of Cholesterol reagent, well mix, incubated for 15 min at RT, then readied against blank standard at 520nm.

2-12 Principle of CHOD/PAP

Cholesterol esterase hydrolyses esterifies cholesterol to free cholesterol, which oxidized to H202,then it react with phenol and 4-Aminoantipyrine to form quinoneimine which is red compound read at 520nm.

2-13 Statistical Analysis

Data analysis was performed using statistical package of social science (SPSS computer program), frequencies, Means, SD, Pearson's correlation have been used to compare and correlate between parameters and study variables.

Chapter Three

Results

Results:

This study included 50 patients under regular hemodialysis (25 male) and (25 female) and 50 control of health people.

In table (3.1) Means of Ages /years (47.84±19.22) for control and (53.04±17.91) for case at P- value = (0.165) and mean of duration/years is (6.26±4.95) at Pvalue 0.165.

In table (3.2) the mean of serum cholesterol was (l62.12±30.49) mg/dl for case is significantly increased compared to control Of healthy people (143.44±38.88), Pvalue was 0.015, and the mean of serum albumin was (3.33±0.51) g/dl for case and it is significantly low in a compare with the mean of control which is (4.22±0.60) g/dl. The p-value was 0.000.

Also the mean of Body Mass Index (BMI) was (20.66±2.87) for case and it is significantly low compared to control which was (25.10±3.65) at P-value 0.00. Referring to table (3.3) the mean of S.cholesterol (l65.44±34.75) mg/dl for male not affect too much more than female which was (l58.80±37.88) mg/dl.

Also mean of S.alb for male was (3.28±0.5) g/dl for male and mean for female was (3.38±0.48) g/dl for the P-value 0.514.

Referring to figure (3.1) there was statically significant negatively correlation between serum Albumin (g/dl) and duration of dialysis /years. (r=-0.314) P-value 0.026

In figure (3.2) S.cholestrol have insignificant positive correlation with duration (r=0.015) at P-value =0.920.

Table (3-1) Means of variation parameters

Variables	**Mean ± SD**	***P- Value***
Age		
Control (50)	47.84 ± 19.22	0.165
Case (50)	53.04 ± 1791	
Duration	6.26 ± 4.95	

Table (3-2) Mean concentrations of S.Alb & S.Chol & BMI among case &control

Parameters	**Control (Mean ± SD)**	**Case (Mean ± SD)**	***P- Value***
S.CHOL (50)	143.44 ± 38.88	162.12±36.13	0.015
S.ALB (50)	4.22 ± 0.60	3.333±0.51	0.000
BMI (50)	25.10 ± 3.65	20.66±2.87	0.000

Table (3-3) Mean of concentrations of S.Alb & S.Chol among gender

Parameters	**Gender**	**Mean ± SD**	***P- Value***
Cholesterol (mg/dl)	Male	165.44±34.75	0.521
	Female	158.80±37.88	
Albumin (g/dl)	Male	3.28±0.55	0.514
	Female	3.38±0.48	

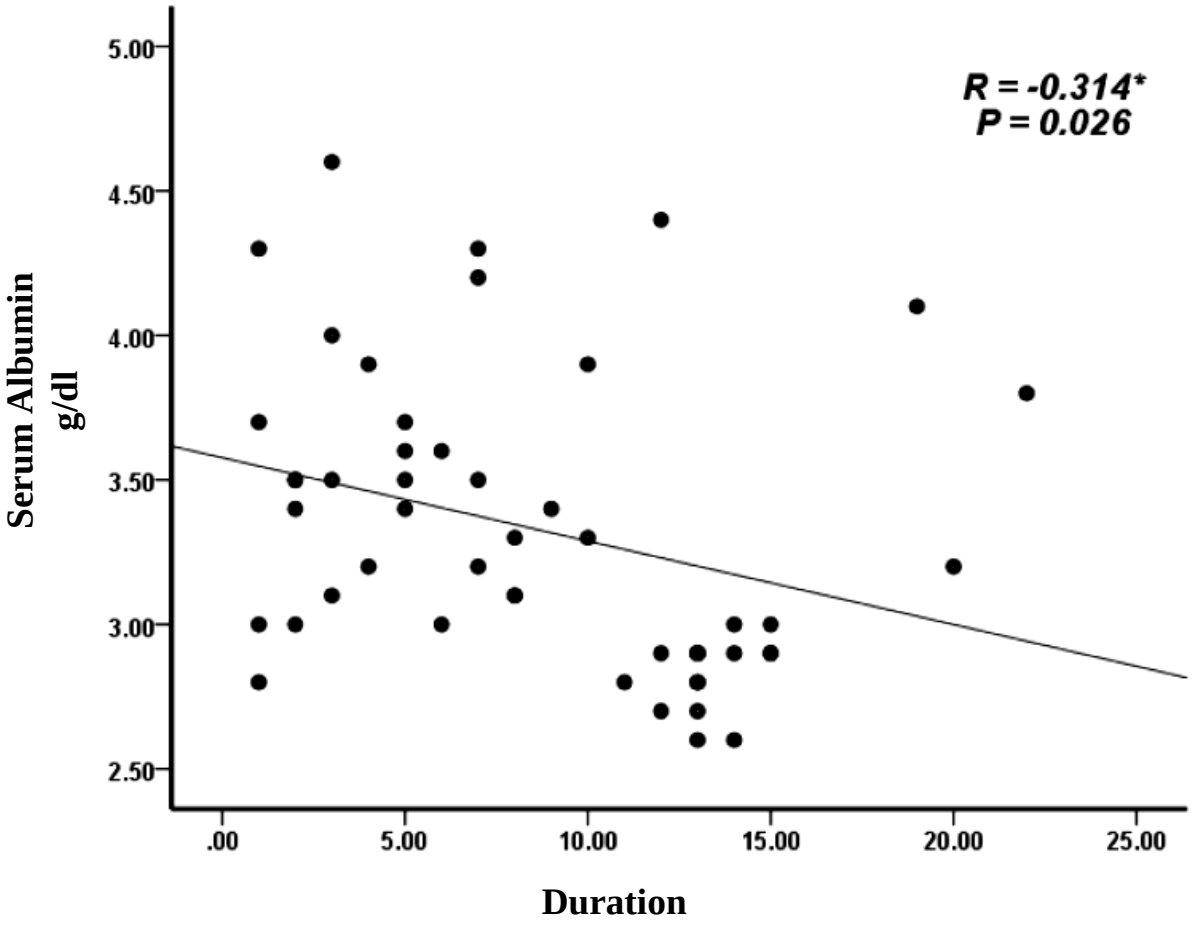
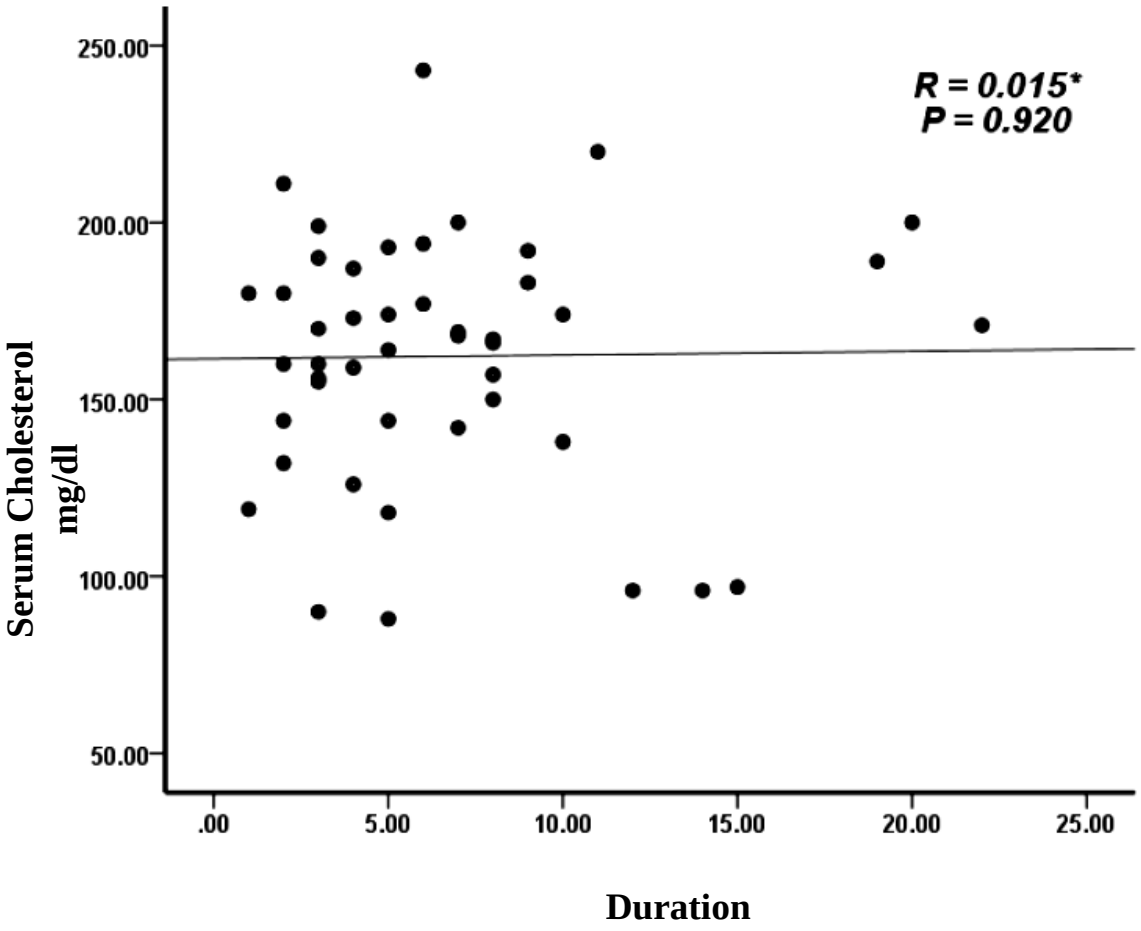


Figure (3-1) correlation between duration and serum Albumin with (R= -0.314, P-value =0.026)



Figure(3.2) correlation between Duration and S. cholesterol (r=0.015 ,P-value =0.920)

Chapter Four

Discussion, Conclusion, Recommendation

4-1 Discussion

The researchers do not believe that there is a single best nutritional marker in a patient with CRD, but that several nutritional markers should be evaluated together According to the national kidney foundation (NKF), serum albumin is the valid indicator of nutritional status in HP, so in each study done to evaluate nutritional state in HP albumin must be followed. Several studies (KoopJe JD.,1997; Qureshi AR et al.,1998; Araujo IC et al .,2006 ; Afshar R et a1.,2007 ; Shegall et al .,2008 ; Bellizzi .V et aJ .,2003) shows that low serum albumin, low serum cholesterol in maintenance hemodialysis patients correlate with increase mortality rate if not treated. In the recent study, we found that patients, under HD are with high serum cholesterol compared to control this finding was in agreement with Sue Huges et al who noted that higher cholesterol levels have been consistently associated with lower mortality levels in patients on dialysis, which is an inverse relationship to that seen in the general population. Also, we found decreased in BMI for the patient which might be more likely to fall ill, and no significant difference in BMI between male and female patients below 40 years was observed, this finding is in agreement with Kurncheu who notice that about 45% of studied patients have a BMI of less than 23.6 a result that suggest a high risk of mortality. Over weight patients have an increase in adipose tissue and are therefore, less likely to suffer from energy deficits and The higher body weight was beneficial for the osseous changes only in females with advanced CRF, while in all other patients no correlation with densitometry parameters.

4-2 conclusion:

From this study it can be concluded that serum albumin was lower in patients under hemodialysis, and there is an inverse association between duration and both serum albumin, and BMI. But serum cholesterol increased with duration of dialysis regardless of gender and age.

4-3 Recommendation

We recommend that for prevention, diagnosis, and treatment of malnutrition for patients with ESRD undergoing hemodialysis, continuous classes should be organized in order to educate patients with chronic renal failure who need hemodialysis about correct nutrition, in addition, periodic nutrition consultations with a dietician and the provision of a detailed diet plan for each patient is very helpful. Conducting similar studies periodically to follow up the nutritional status of patients and the success rate of interventions.

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Appendix (1)

Sudan University of Science and technology

College of Graduate studies

M.SC of medical laboratory

Questionnaire:

No …….

Name …….

Age…….

Sex…….

Weight…….

Duration…….

Other disease…….

Original state…….

Laboratory investigation

Serum Albumin …….g/dl

Serum Cholesterol …….mg/dl

ACE	Angiotensin Converting Enzyme
APD	Automated Peritoneal Dialysis
BMI	Body Mass Index
CAPD	Continuous Ambulatory Peritoneal Dialysis
CKD	Chronic Kidney Disease
CKD5	Chronic Kidney Disease stage 5
CRP	C-reactive protein
CT	Connective tissue
CVD	Cardio- vascular disease
DCI	Dailey Calorie Intake
DPI	Dailey Protein Intake
ECF	Extra cellular fluid
EPO	Erythropoietin
ESDR	End Stage Renal Disease
GFR	Glomerular filtration rate
HD	Hemodialysis
HDP	Hemodialysis patients
IL-6	Interleukin-6
IPD	Intermittent Peritoneal Dialysis
MIA	Malnutrition Inflammation Atherosclerosis syndrome
NKF	National kidney foundation
PEM	Protein-energy malnutrition
PEW	Protein-energy wasting
RCC	Renal cell carcinoma
RRT	Renal replacement therapy
RVT	Renal vein thrombosis

Reagents for measurement of albumin concentration
Only for *in vitro* use in the clinical laboratory

CE

ALBUMIN BROMOCRESOL GREEN

PRINCIPLE OF THE METHOD

Albumin in the sample reacts with bromocresol green in acid medium forming a coloured complex that can be measured by spectrophotometry[1].

PRESENTATION

	[illegible]	225 1.073
A. Reagent S. Standard	2 x 250 mL 1 x 5 mL	1 x 250 mL 1 x 5 mL

COMPOSITION

A. Reagent: Acetate buffer 100 mmol/L, bromocresol green 0.27 mmol/L, detergent, pH 4.1.

S. Albumin Standard: Bovine albumin. Concentration is given on the label. Concentration value is traceable to the Standard Reference Material 927 (National Institute of Standards and Technology, USA).

STORAGE

Reagent (A): Store at 2-8°C.

Albumin Standard (S): Store at 2-8°C, once opened.

Reagent and Standard are stable until the expiry date shown on the label when stored tightly [illegible] ar[illegible] prevent[illegible] [illegible] indications of deterioration:

– Reagent: Presence of particulate material, turbidity, absorbance of the blank over 0.200 at 630 nm (1 cm cuvette).

– Standard: Presence of particulate material, turbidity.

REAGENT PREPARATION

Reagent and Standard are provided ready to use.

ADDITIONAL EQUIPMENT

– Analyzer, spectrophotometer or photometer able to read at 630 nm (610 - 670 nm).

SAMPLES

Serum or plasma (EDTA, citrate or heparine) collected by standard procedures.

Albumin in serum is stable for 3 days at 2-8°C.

PROCEDURE

1. Pipette into labelled test tubes: (Notes 1, 2)

	Blank	Standard	Sample
Albumin Standard (S)	—	10 µL	—
Sample	—	—	10 µL
Reagent (A)	1.0 mL	1.0 mL	1.0 mL

2. Mix thoroughly and let stand the tubes for 1 minute at room temperature.
3. Read the absorbance (A) of the Standard and the Sample at 630 nm against the Blank. The colour is stable for 30 minutes.

CALCULATIONS

The albumin concentration in the sample is calculated using the following general formula:

$$\frac{A\ Sample}{A\ Standard} \times C\ Standard = C\ Sample$$

REFERENCE VALUES

Serum[2]:

Newborn, 2 to 4 days	28-44 g/L
4 days to 14 years	38-54 g/L
Adult	35-50 g/L
> 60 years	34-48 g/L

These ranges are given for orientation only; each laboratory should establish its own reference ranges.

QUALITY CONTROL

It is recommended to use the Biochemistry Control Serum level I (cod. 18005, 18009 and 18042) and II (cod. 18007, 18010 and 18043) to verify the performance of the measurement procedure.

Each laboratory should establish its own internal Quality Control scheme and procedures for corrective action if controls do not recover within the acceptable tolerances.

METROLOGICAL CHARACTERISTICS

– Detection limit: 1.1 g/L.

– Linearity limit: 70 g/L.

– Reproducibility (within run):

Mean Concentration	CV	n
26.2 g/L	1.4 %	20
42.1 g/L	1.0 %	20

– Reproducibility (run to run):

Mean Concentration	CV	n
26.2 g/L	1.9 %	25
42.1 g/L	1.9 %	25

– Trueness: Results obtained with this reagent did not show systematic differences when compared with reference reagents (Note 3). Details of the comparison experiments are available on request.

– Interferences: Bilirubin (>10 mg/dL), lipemia (triglycerides >7.5 g/L) and hemoglobin (>2.5 g/L) may affect the results. Other drugs and substances may interfere[3].

These metrological characteristics have been obtained using an analyzer. Results may vary if a different instrument or a manual procedure is used.

DIAGNOSTIC CHARACTERISTICS

Albumin is the most abundant protein in human plasma. It has three main functions: it contributes towards maintaining the colloid oncotic pressure of plasma, it acts as non-specific transport vehicle for many nonpolar compounds and it is a source of endogenous amino acids.

Hyperalbuminemia is of little diagnostic significance except in dehydration[2].

Hypoalbuminemia is found as a result of several factors: reduced synthesis caused by liver diseases; reduced absorption of amino acids due to malabsorption syndromes or malnutrition; increased catabolism as a result of inflammation or tissue damage; altered distribution between intravascular and extravascular space due to increased capillary permeability, overhydration or ascites; abnormal losses caused by renal disease (nephrotic syndrome, diabetes mellitus, chronic glomerulonephritis, systemic lupus erythematosus), gastrointestinal tract disease (ulcerative colitis, Crohn's disease) or skin damage (exfoliative dermatitis, extensive burns); congenital absence of albumin or analbuminemia[2,4].

Albumin plasma concentrations, although important for management and follow-up, have very little value in diagnosis[2].

Clinical diagnosis should not be made on the findings of a single test result, but should integrate both clinical and laboratory data.

NOTES

1. This reagent may be used in several automated analysers. Instructions for many of them are available on request.
2. Albumin reaction with bromocresol green is immediate. It is not recommended to delay readings, since other proteins react slowly.
3. Calibration with the provided aqueous standard may cause a matrix related bias, specially in some analyzers. In these cases, it is recommended to calibrate using a serum based standard (Biochemistry Calibrator, cod. 18011 and 18044).

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Reactivo para medida colorimétrica de albúmina
Sólo para uso in vitro en el laboratorio clínico

CE

ALBÚM
VERDE DE BROMOCRES

FUNDAMENTO DEL MÉTODO

La albúmina presente en la muestra reacciona con el verde de bromocresol en medio ácido, originando un complejo coloreado que se cuantifica por espectrofotometría[1].

CONTENIDO

	COD 11547	COD 11573
A. Reactivo	2 x 250 mL	1 x 250 mL
S. Patrón	1 x 5 mL	1 x 5 mL

COMPOSICIÓN

A. Reactivo. Tampón acetato 100 mmol/L, verde de bromocresol 0,27 mmol/L, detergente, pH 4,1.

S. Patrón de Albúmina. Albúmina bovina. La concentración viene indicada en la etiqueta. El valor de concentración es trazable al Material de Referencia Certificado 927 (National Institute of Standards and Technology, USA).

CONSERVACIÓN

Reactivo (A): Conservar a 2-8ºC.

Patrón de Albúmina (S): Conservar a 2-8ºC, una vez abierto.

El Reactivo y el Patrón son estables hasta la fecha de caducidad indicada en la etiqueta, siempre que se conserven bien cerrados y se evite la contaminación durante su uso.

Indicaciones de deterioro

- Reactivo: Presencia de partículas, turbidez, absorbancia del blanco superior a 0,200 a 630 nm (cubeta de 1 cm).
- Patrón: Presencia de partículas o turbidez.

PREPARACIÓN DE LOS REACTIVOS

Tanto el Reactivo como el Patrón están listos para su uso.

EQUIPO ADICIONAL

- Analizador, espectrofotómetro o fotómetro para lecturas a 630 nm (610 - 670 nm).

MUESTRAS

Suero o plasma (EDTA, heparina o citrato) recogido mediante procedimientos estándar.
La albúmina en suero es estable durante 3 días a 2-8ºC.

PROCEDIMIENTO

1. Pipetear en tubos de ensayo: (Notas 1, 2)

	Blanco	Patrón	Muestra
Patrón Albúmina (S)	—	10 µL	—
Muestra	—	—	10 µL
Reactivo (A)	1,0 mL	1,0 mL	1,0 mL

2. Agitar bien y dejar los tubos durante 1 minuto a temperatura ambiente.
3. Leer la absorbancia (A) del Patrón y de la Muestra a 630 nm frente al Blanco. El color es estable durante al menos 30 minutos.

CÁLCULOS

La concentración de albúmina en la muestra se calcula a partir de la siguiente fórmula general:

$$\frac{A\ Muestra}{A\ Patrón} \times C\ Patrón = C\ Muestra$$

VALORES DE REFERENCIA

Suero[2]:

Recién nacidos, 2 a 4 días	28-44 g/L
4 días a 14 años	38-54 g/L
Adultos	35-50 g/L
> 60 años	34-48 g/L

Estos valores se dan únicamente a título orientativo; es recomendable que cada laboratorio establezca sus propios intervalos de referencia.

CONTROL DE CALIDAD

Se recomienda el uso de los Sueros Control Bioquímica niveles I (cod. 18005, 18009 y 18042) y II (cod. 18007, 18010 y 18043), para verificar la funcionalidad del procedimiento de medida.

Cada laboratorio debe establecer su propio programa de Control de Calidad interno, así como procedimientos de corrección en el caso de que los controles no cumplan con las tolerancias aceptables.

CARACTERÍSTICAS METROLÓGICAS

- Límite de detección: 1,1 g/L.
- Límite de linealidad: 70 g/L.
- Repetibilidad (intraserie):

Concentración media	CV	n
26,2 g/L	1,4 %	20
42,1 g/L	1,0 %	20

- Reproducibilidad (interserie):

Concentración media	CV	n
26,2 g/L	1,9 %	25
42,1 g/L	1,9 %	25

- Veracidad: Los resultados obtenidos con estos reactivos no muestran difere sistemáticas significativas al ser comparados con reactivos de referencia (Nota 3) detalles del estudio comparativo están disponibles bajo solicitud.
- Interferencias: La bilirrubina (>10 mg/dL), la lipemia (triglicéridos >7,5 g/L) y la hemogl (> 2,5 g/L) pueden afectar los resultados. Otros medicamentos y sustancias pu interferir[3].

Estos datos han sido obtenidos utilizando un analizador. Los resultados pueden vari cambiar de instrumento o realizar el procedimiento manualmente.

CARACTERÍSTICAS DIAGNÓSTICAS

La albúmina es la proteína más abundante en el plasma humano. Tiene tres funci principales: contribuye en el mantenimiento de la presión oncótica del plasma, actúa c transportador no específico para muchos componentes apolares y es una fuente endógen aminoácidos.

La hiperalbuminemia tiene poco significado diagnóstico excepto en la deshidratación[2].

La hipoalbuminemia se encuentra como resultado de diversos factores: síntesis redu causada por enfermedades hepáticas; absorción reducida de aminoácidos debida a síndro de malabsorción o malnutrición; aumento del catabolismo como consecuencia de inflamaci daño tisular; distribución alterada entre el espacio intravascular y extravascular causada permeabilidad capilar aumentada, sobrehidratación o ascitis; pérdidas anormales debid enfermedades renales (síndrome nefrótico, diabetes mellitus, glomerulonefritis crónica, l eritematoso sistémico), enfermedades del tubo digestivo (colitis ulcerativa, enfermedad Crohn) o alteraciones de la piel (dermatitis exfoliativa, quemadas extensas); ausencia congé de albúmina o analbuminemia[2,4].

Las concentraciones plasmáticas de albúmina, aunque importantes para el contro seguimiento, tienen muy poco valor diagnóstico[2].

El diagnóstico clínico no debe realizarse teniendo en cuenta el resultado de un único ensa sino que debe integrar los datos clínicos y de laboratorio.

NOTAS

1. Estos reactivos pueden utilizarse en la mayoría de analizadores automáticos. Soli información a su distribuidor.
2. La reacción de la albúmina con el verde de bromocresol es inmediata. Se recomienda demorar las lecturas, ya que otras proteínas reaccionan lentamente.
3. La calibración con el patrón acuoso suministrado puede causar sesgos, especialmente algunos analizadores. En estos casos, se recomienda calibrar usando un patrón de bi sérica (Calibrador Bioquímica, cod. 18011 y 18044).

BIBLIOGRAFÍA

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SPECTRUM

Cholesterol – Liquizyme CHOD-PAP *(Single Reagent)*

REF: 230 001	(2 x 25 ml)	50 test
REF: 230 002	(4 x 25 ml)	100 test
REF: 230 003	(4 x 30 ml)	120 test
REF: 230 004	(5 x 15 ml)	100 test
REF: 230 005	(4 x 50 ml)	200 test
REF: 230 006	(4 x 100 ml)	400 test
REF: 230 007	(8 x 100 ml)	800 test
REF: 230 008	(6 x 100 ml)	600 test
REF: 230 009	(2 x 500 ml)	1000 test
REF: 230 010	(4 x 250 ml)	1000 test
REF: 230 011	(5 x 100 ml)	500 test

Intended Use

Spectrum Diagnostics liquizyme cholesterol reagent is intended for in-vitro quantitative, diagnostic determination of cholesterol in human serum on both manual and automated systems.

Background

Measurement of serum cholesterol levels is important as an indicator of liver function, intestinal absorption, biliary function and in the diagnosis and classification of hyperlipoproteinemias.
Elevated cholesterol levels may occur with hypothyroidism, diabetes and nephrotic syndrome. Elevated serum cholesterol levels correlate well with the incidence of coronary artery diseases. Stress, age, gender, hormonal balance and pregnancy affect normal cholesterol levels. Depressed levels are associated with hyperthyroidism and severe liver diseases.

Method

CHOD-PAP-enzymatic colorimetric method.

Assay Principle

The series of the reactions involved in the assay system is as follows:

1. Cholesterol esters are enzymatically hydrolyzed by cholesterol esterase (CE) to cholesterol and free fatty acids.

2. Free cholesterol, including that originally present, is then oxidized by cholesterol oxidase (CO) to cholest-4-en-3-one and hydrogen peroxide.

3. The hydrogen peroxide combines with phenol and 4-amino-antipyrine (4AAP) in the presence of peroxidase (POD) to form a chromophore (quinoneimine dye) which may be quantitated at 500 – 550 nm. For bichromatic analyzers the blank wavelength should be set to 600 or 650 nm.

Reagents

Standard cholesterol (ST)		
200 mg/dL	5.17	mmol/L
Reagent (R)		
Pipes Buffer pH 7.0	50	mmol/L
Phenol	30	mmol/L
Sodium cholate	5.0	mmol/L
Cholesterol esterase	>250	U/L
Cholesterol oxidase	>500	U/L
Peroxidase	>2.0	KU/L
4-amino-antipyrine	1.0	mmol/L
Sodium Azide	8.0	mmol/L

For further information, refer to the Cholesterol reagent material safety data sheet.

SYMBOLS IN PRODUCT LABELLING	
EC REP Authorised Representative	Temperature Limitation
IVD For in-vitro diagnostic use	Use by/Expiration Date
LOT Batch Code/Lot number	CAUTION, Consult instructions
REF Catalogue Number	Use once
Consult instructions for use	Manufactured by

Precautions and Warnings

Do not ingest or inhalate. In case of contact with eyes or skin; rinse immediately with plenty of soap and water. In case of severe injuries; seek medical advice immediately.

Reagent (R) contains sodium azide which may react with copper or lead plumbing.

Reagent Preparation, Storage and Stability

Spectrum cholesterol reagents are ready to use. They are stable up to the expiry date labeled on the bottles. Once opened, the opened vial is stable for 3 months at 2 - 8 °C.

Deterioration

The reagent is normally clear or pale pink. Do not use liquizyme cholesterol reagent if it is turbid or if the absorbance is greater than 0.15 at 546 nm.

Specimen Collection and Preservation

It is recommended that prior to sample collection, patients should be following their usual diet and be in their usual state of health. Patients who are actually ill, losing weight, pregnant or have had a myocardial infarction in the previous 3 months should be rescheduled. Both fasting and non fasting samples can be used. Non haemolysed serum or plasma can be stored at 4 °C up to 7 days prior to analysis, 5-7 days at 20-25°C, stable for 3 months at -20 °C, and at -70 °C for several months. The only acceptable anticoagiulant is heparin.

System Parameters

Wavelength	546 nm (500 – 550 nm)
Optical path	1 cm
Assay type	End-point
Direction	increase
Sample : Reagent Ratio	1 : 100
e.g .: Reagent volume	1 ml
Sample volume	10 µl
Temperature	15 – 25 °C or 37 °C
Zero adjustment	Reagent blank
Incubation time	5 minutes at 37 °C or 10 minutes at 15 – 25 °C
Reagent Blank Limits	Low 0.00 AU High 0.15 AU
Sensitivity	5 mg/dL (0.13mmol/L)
Linearity	750 mg/dL (19.5 mmol/L)

Procedure

	Blank	Standard	Sample
Reagent (R)	1.0 ml	1.0 ml	1.0 ml
Standard	.....	10 µl	.....
Sample	.....	.....	10 µl

Mix and incubate for 5 minutes at 37 °C or 10 minutes at 15 – 25 °C. Measure absorbance of specimen ($A_{specimen}$) and standard ($A_{standard}$) against reagent blank within 30 minutes.

Calculation

$$\text{Serum cholesterol conc. (mg/dL)} = \frac{(A_{specimen})}{(A_{standard})} \times 200$$

Quality Control

Normal & abnormal commercial control serum of known concentrations should be analyzed with each run.

Performance Characteristics

Precision

Within run (Repeatability)

	Level 1	Level 2
n	20	20
Mean (mg/dL)	149.8	252
SD	1.69	1.91
CV%	1.13	0.76

Run to run (Reproducibility)

	Level 1	Level 2
n	20	20
Mean (mg/dL)	157	259
SD	1.77	2.12
CV%	1.23	0.97

Methods Comparison

A comparison between Spectrum Diagnostics Cholesterol reagent and a commercial reagent of the same methodology was performed on 20 human sera. A correlation of 0.988 was obtained.

Sensitivity

When run as recommended, the minimum detection limit of the assay is 5 mg/dL (0.13 mmol/L).

Linearity

The reaction is linear up to a cholesterol concentration of 750 mg/dl; specimens showing higher concentration should be diluted 1+1 using physiological saline and repeat the assay (result × 2).

Interfering Substances:

Haemolysis
No significant interference up to a level of 500 mg/dl.

Icterus
No interference from free bilirubin up to a level of 15 mg /dL (260 mmol/L) and conjugated bilirubin up to a level of 7 mg/dL (116 mmol/L).

Lipemia
No significant interference up to 1.7 AU.

Drugs
Of the drugs tested in vitro, methyldopa causes artificially Low total cholesterol values at the tested drug Level.

Others
Physiological ascorbic acid concentration does not interfere with the test. Ascorbic Acid levels higher than 425 mmol/l (7.5 mg/dl) decrease the apparent total cholesterol concentration significantly.

Expected Values

The following guidelines may be used for clinical interpretation:

Risk classification	Total cholesterol	
Desirable	<200 mg/dl	<5.2 mmol/L
Borderline high	200-239 mg/dl	5.2-6.2 mmol/L
High	≥240 mg/dl	≥6.2 mmol/L

Spectrum Diagnostics does not interpret the results of a t laboratory procedure; interpretation of the reults is cons the responsibility of qualified medical personnel. All indic of clinical significance are supported by literature refere

Dynamic Range

5 - 750 mg/dl (0.13 - 19.5 mmol/L)

Waste Disposal

This product is made to be used in professional laboratorie Please consult local regulations for a correct waste disposa
S56: dispose of this material and its container at hazardous special waste collection point.
S57: use appropriate container to avoid environmental contam
S61: avoid release in environment. refer to special instruction data sheets.

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ORDERING INFORMATION	
CATALOG NO.	QUANTITY
230 001	2 x 25 ml
230 002	4 x 25 ml
230 003	4 x 30 ml
230 004	10 x 15 ml
230 005	4 x 50 ml
230 006	4 x 100 ml
230 007	8 x 100 ml
230 008	6 x 100 ml
230 009	2 x 500 ml
230 010	4 x 250 ml
230 011	5 x 100 ml

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