STUDY OF THE ASSOCIATION BETWEEN PROTEIN ENERGY WASTING (PEW) AND PSOAS MUSCLE INDEX (PMI) IN PATIENTS WITH CHRONIC KIDNEY DISEASE

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

DOCTORATE OF MEDICINE (DM)

(NEPHROLOGY)

JUNE, 2022 **DR. MAHENDRA KUMAR JANGID**

AIIMS, JODHPUR

STUDY OF THE ASSOCIATION BETWEEN PROTEIN ENERGY WASTING (PEW) AND PSOAS MUSCLE INDEX (PMI) IN PATIENTS WITH CHRONIC KIDNEY DISEASE

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

DOCTORATE OF MEDICINE (DM)

(NEPHROLOGY)

JUNE, 2022 **DR. MAHENDRA KUMAR JANGID**

AIIMS, JODHPUR

All India Institute of Medical Sciences, Jodhpur

DECLARATION

I hereby declare that the thesis titled "**Study Of the association between Protein Energy Wasting (PEW) and Psoas Muscle Index (PMI) in patients with Chronic Kidney Disease**" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

Dr Mahendra Kumar Jangid
Department of Nephrology
All India Institute of Medical Sciences
Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "**Study Of the association between Protein Energy Wasting (PEW) and Psoas Muscle Index (PMI) in patients with Chronic Kidney Disease**" is the bonafide work of Dr Mahendra Kumar Jangid carried out under our guidance and supervision, in the Department of Nephrology, All India Institute of Medical Sciences, Jodhpur.

Supervisor

Dr Manish Chaturvedy

Additional Professor and Head of Department

Department of Nephrology

AIIMS, Jodhpur

Co-Supervisor

Dr. Praveen Sharma
Professor
Department of Biochemistry
AIIMS,Jodhpur

Co-Supervisor

Dr. Nitin Kumar Bajpai
Associate Professor
Department of Nephrology
AIIMS,Jodhpur

Co-Supervisor

Dr. Pawan Kumar Garg
Associate Professor
Department of Radiology
AIIMS,Jodhpur

All India Institute of Medical Sciences, Jodhpur

CERTIFICATE

This is to certify that the thesis titled "**Study Of the association between Protein Energy Wasting (PEW) and Psoas Muscle Index (PMI) in patients With Chronic Kidney Disease**" is the bonafide work of Dr Mahendra Kumar Jangid carried out under our guidance and supervision, in the Department of Nephrology, All India Institute of Medical Sciences, Jodhpur.

Dr Manish Chaturvedy
Additional Professor & Head of Department
Department of Nephrology
AIIMS, Jodhpur

ACKNOWLDGEMENT

I would like to acknowledge everyone who played a role in my academic accomplishments.

Foremost I would like to express my sincere gratitude to my guide Dr. Manish chaturvedy ,Additional Professor and Head of Department of Nephrology for his trust on my abilities, patience, motivation, ideas, support and immense knowledge. I am extremely thankful and indebted to him for sharing expertise, sincere and valuableguidance and encouragement extended to me at all times of crisis.

I am deeply indebted to my co-guides, Dr. Praveen Sharma, Professor, Department of Biochemistry for extending the sincere support in conducting blood biochemistry tests analysis and guidance. I extend my heartfelt thanks to Dr. Pawan Kumar Garg, Associate Professor, Department of Radiodiagnosis, for mentoring me and helping me in every step of my dissertation. I would like to recognize the invaluable assistance that you provided during my study. I would like to extend my gratitude to Dr. Nitin Kumar Bajpai, Associate Professor, Department of Nephrology, who has been vital to my technical aspects of thesis and his experience in taking up this topic for study. I would like to extend my gratitude to Dr. Akhil Dhanesh Goel, Assistant Professor, Department of community medicine for assistance for application of statistical measures in my thesis, I am indebted to the help of Dr. Rajesh Jhorawat Associate Professor, Department of Nephrology, for his sincere help in the making of thesis and making it better for submission.

I thank my patients, the greatest teachers without whom my knowledge, experience and dissertation would have been incomplete.

I would like to express my profound gratitude to my parents, Mr. Chhuttan Lal Jangid & Mrs. Shanti Devi and I wish to acknowledge the support and great love of my wife Mrs. Priyanka Sharma for providing me with unceasing encouragement, support and attention throughout my years of life, study and career. This accomplishment would not have been possible without them, and I know I always have my family to count on constantly when times are rough.

I am thankful to my seniors Dr. C. Malswamkima & Dr. Jony Agrawal who helped me in every step of my dissertation with their immense experience and knowledge.

A good supporting system is important for survival and staying sane. I would like to thank my dear colleagues Dr. Santosh Maurya for his unwavering support, fruitful discussions, guidance and insightful suggestions which paved way forward at times of trouble and whose assistance was a milestone in the completion of my thesis.

I would like to thank my juniors Dr. Santosh Kumar V, Dr. Ambar, Dr. Bipin, Dr. Tapabrata Das & Dr. Uttayan for their assistance and support.

Great friends are the best asset for any fortunate individual. My best friend Dr. Pawan Kumar was very vital for the journey which stands at this point in my career.

I would also like to offer my thanks to of Department of Radiology and Biochemistry, AIIMS Jodhpur for the proper management of patients coming to OPD, coordination, blood reports and helping in preventing distress to patient which can occur during the conduct of thesis.

All the faculties and senior residents of the Department of Nephrology, All India Institute of Medical Sciences, Jodhpur have been pillars of support and understanding and this would not have been possible without them.

Dedicated to my family

INDEX

LIST OF ABBREVIATIONS

CKD	:	CHRONIC KIDNEY DISEASE
ESRD	:	END STAGE RENAL DISEASE
CTIN	:	CHRONIC TUBULO-INTERSTITIAL NEPHRITIS
CGN	:	CHRONIC GLOMERULONEPHRITIS
BMI	:	BODY MASS INDEX
MAMC	:	MID-ARM MUSCLE CIRCUMFERENCE
KDOQI	:	KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE
KDIGO	:	KIDNEY DISEASE: IMPROVING GLOBAL OUTCOMES
Hb	:	HEMOGLOBIN
HD	:	HEMODIALYSYIS
PMI	:	PSOAS MUSCLE INDEX
SGA	:	SUBJECTIVE GLOBAL ASSESEMENT
PEW	:	PROTEIN ENERGY WASTING
PMTH	:	PSOAS MUSCLE THICKNESS HEIGHT
DEI	:	DAILY ENERGY INTAKE
DPI	:	DAILY PROTEIN INTAKE
BIA	:	Bioelectrical impedance analysis
BPH	:	BENIGN PROSTATIC HYPERPLASIA
DXA	:	Dual-energy X-ray absorptiometry
CC	:	Calf circumstances
CI	:	Creatinine index

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death.

Definition of Chronic Kidney Disease Criteria

1. Kidney damage for 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR that can lead to decreased GFR, manifest by either : -

- Pathological abnormalities; or
- Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests

2. GFR <60 mL /min/1.73 m2 for ≥3 months, with or without kidney damage [1].

Stage	Description	GFR (ml/min/1.73m²)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney failure	<15

Table no.1 Schematic representation of Stages of Chronic Kidney Disease.

Sarcopenia was a term coined by Irwin Rosenberg to mean ‘paucity of flesh’ (in Greek ‘sarx’ or flesh + ‘penia’ or loss). It refers to age-related decline in skeletal muscle [2]. A seemingly simple construct of age-related decline in skeletal muscle has been met by a plethora of operational definitions. To date, the term sarcopenia is primarily a research term.

However, the recent development of an International Classification of Diseases, 10th Revision (ICD-10) code for sarcopenia highlights the need for uniformity and recognition of the underlying constructs by practicing clinicians. Age-related decline in skeletal muscle is confounded by disease, with estimates as high as 92% of older adults having at least one chronic disease [3]. Therefore, the definition of sarcopenia was adapted to include any loss of muscle tissue and function due to aging, chronic diseases (including cancer), low protein energy intake and physical inactivity. Chronic kidney

disease (CKD) is a catabolic state, known to be associated with protein wasting and with multiple metabolic derangements due to uraemia. In addition, there may also be decreased muscle synthesis in the uremic milieu.

Protein-energy wasting (PEW) is common in patients with chronic kidney disease (CKD).

PEW is one of the strongest predictors of mortality in patients with CKD.

Prevalence of PEW is 28% to 54% among 16434 adults undergoing maintenance dialysis. PEW prevalence increases when renal function declines, that is, from <2% in CKD stages 1–2 to 11–54% in CKD stages 3–5. A more general definition of cachexia for all chronic diseases proposed by the Society on Sarcopenia, Cachexia and Wasting Disorders was also published concurrently. In the CKD area, we found 180 publications using ‘cachexia’ underlining that some confusion or overlap may exist. The definitions of PEW and cachexia are somewhat similar, and the main difference is that a loss of body weight >5% is a mandatory criterion for cachexia but supportive for PEW[4]

The International Society of Renal Nutrition and Metabolism (ISRNM) expert panel has defined PEW as a, “state of decreased body stores of protein and energy fuels (body protein and fat masses)”. The ISRNM panel has also proposed diagnostic criteria of PEW with four categories. Cachexia is a severe form of PEW. The proposed causes of PEW are multi-factorial and include nutritional and non-nutritional mechanisms.

Causes of PEW in CKD Patients (adopted from [5]

1. Decrease protein and energy intake
    a. Anorexia
        i. Dysregulation in circulating appetite mediators
        ii. Hypothalamic amino acid sensing
        iii. Nitrogen-based uremic toxins
    b. Dietary restrictions
    c. Alterations in organs involved in nutrient intake
    d. Depression
    e. Inability to obtain or prepare food
2. Hypermetabolism
    a. Increased energy expenditure
        i. Inflammation
        ii. Increased circulating pro-inflammatory cytokines
        iii. Insulin resistance secondary to obesity
        iv. Altered adiponectin and resistin metabolism
    b. Hormonal disorders
        i. Insulin resistance
        ii. Increased glucocorticoid activity
3. Metabolic acidosis
4. Decreased physical activity
5. Decreased anabolism
    a. Decreased nutrient intake
    b. Resistance to GH/IGF-1
    c. Testosterone deficiency
    d. Low thyroid hormone levels
6. Comorbidities and lifestyle
    a. Comorbidities (diabetes, CHF, depression, coronary artery disease, peripheral vascular disease)
7. Dialysis
    a. Nutrient losses into dialysate
    b. Dialysis-related inflammation
    c. Dialysis-related hypermetabolism & Loss of residual renal function

Muscle wasting, i.e., the loss of muscle mass, is prevalent in patients with end-stage kidney disease undergoing haemodialysis. Muscle wasting is a result of a negative protein balance caused by inflammation, increased protein catabolism, and insufficient energy and protein intake [6] .
Thus, muscle wasting may be a common component of protein energy wasting which is defined as a loss of muscle and fat mass due to chronic inflammation, or sarcopenia which is characterized by low skeletal muscle mass with low muscle function.

Haemodialysis (HD) is one of most commonly used dialysis modalities in end-stage renal disease patients requiring renal replacement therapy. With advances in HD technologies and cares, the survival of HD patients has improved. However, the prevalence of long-term complications increased over time with treatment and as the dialysis population ages.

(1) Decreased muscle mass is one complication that can develop in long-term HD patients.

(2) This is associated with decreased quality of life and increased morbidity or mortality in HD Patients.

(3) Therefore, accurate muscle mass measurement is important for predicting prognosis or physical performance in HD patients.

Computed tomography (CT) and dual X-ray absorptiometry (DXA) are commonly used for measuring muscle mass in HD patients (4, 5). Previous studies have shown that, among various muscle mass indices, the psoas muscle (PM) index measured on CT is associated with clinical outcomes in HD patients.

Both protein energy wasting and sarcopenia are prevalent and associated with increased mortality in patients undergoing haemodialysis Because muscle function, muscle strength, and physical performance are generally low in patients undergoing haemodialysis, the precise measurement of muscle mass is clinically important.

Surrogate methods such as bioelectrical impedance analysis and dual-energy X-ray absorptiometry are available in clinical practice; however, the accuracy of these methods can be affected by the patient's hydration status [7]. Thus, the European Consensus Statement recommends computed tomography (CT) as the gold standard method for the assessment of muscle mass, as it is not affected by hydration status.

Several previous studies have reported that CT-measured indices such as the abdominal skeletal muscle index and psoas muscle mass index at the level of the third lumbar vertebra (L3) are widely used to diagnose sarcopenia or muscle wasting and predict mortality in patients with various cancers and chronic liver disease[4] [8 ,9]. However, specialized software, multiple attempts, and specific technical skills are required to measure these indices. Recently, CT-measured psoas muscle thickness per height (PMTH), defined as the largest transverse diameter of the right psoas muscle standardized for height, has been introduced as a simple measurable indicator of skeletal muscle mass for predicting mortality in patients with advanced liver disease [10,11].

There are various studies in relation of clinical significance of defining role of PMI/PMTH in liver cirrhosis, colon carcinoma and other malignancies to predict morbidity and mortality but in CKD no sufficient studies are done in relation with clinical significance of PMI/PMTH and its association with other biochemical parameters and to predict disease progression and morbidity in patient with CKD. However, in the field of nephrology, the use of CT for body composition analysis is limited owing to radiation exposure and high costs.

Only a few studies have examined the association between CT-measured sarcopenia indices and mortality in patients undergoing hemodialysis [12,13]. Although the use of PMTH for predicting mortality remains unclear in population with chronic kidney disease. It is clinically important to consider the pathophysiology which brings to lowering PMTH, therefore the relationships between PMTH and baseline variables were examined. Moreover, the present study aimed to investigate association between protein energy wasting (PEW) and CT-measured PMTH/-PMI in patients with CKD.

REVIEW OF LITERATURE

Chronic kidney disease (CKD) is a global health issue, since 11–13% of the world population can be diagnosed with CKD in different severity stages [14]. The syndrome is characterized by several nutritional and metabolic derangements, that become clinically evident in most advanced stages.

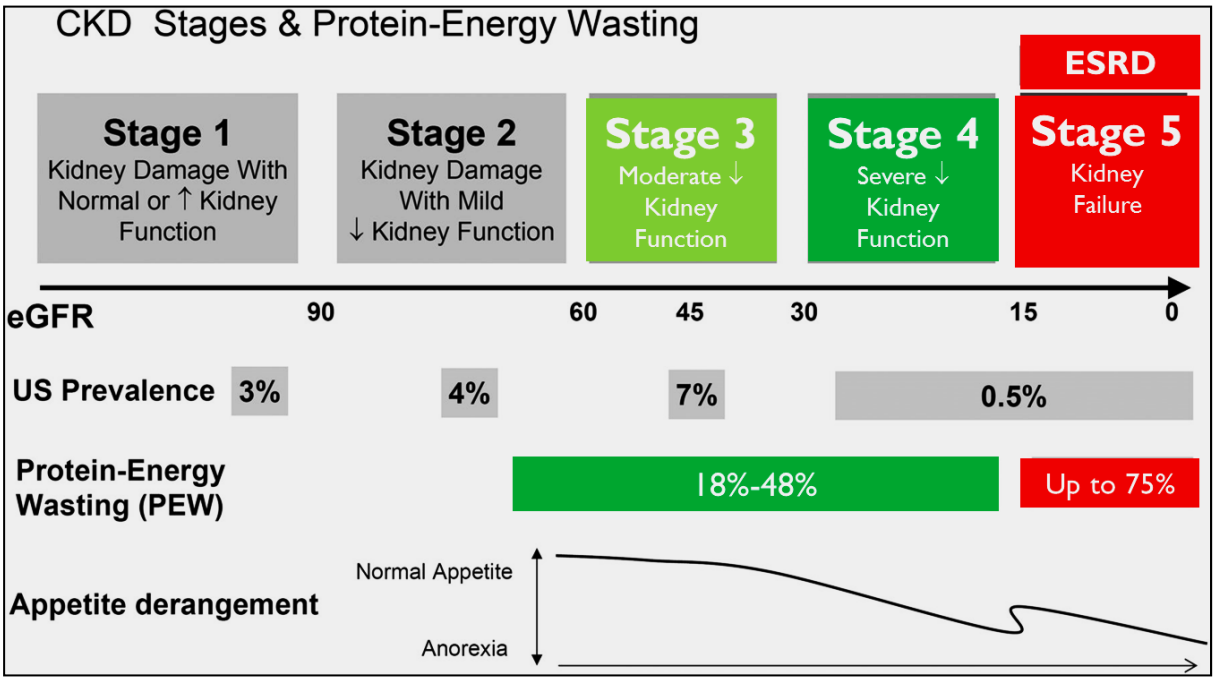


Fig no.1 shows development of protein-energy wasting with advancing stages of chronic kidney disease.

Protein energy wasting (PEW) represents one of the most serious complications of chronic kidney disease (CKD) [15] and poses a formidable therapeutic challenge because

(a) it is common and is frequently encountered not only in individuals with end stage renal disease (ESRD) who are receiving maintenance haemodialysis (HD) or chronic peritoneal dialysis (PD) therapy but also in non-dialyzed patients with CKD;

(b) it is caused by a wide range of disorders or factors that may or may not be related directly to the underlying kidney disease [16]

(c) it can cause severe and prolonged debilitation leading to poor quality of life. In addition, PEW assumes an even greater significance because it often coexists with other co-morbid risk factors, such as diabetes, inflammation, and atherosclerosis, and is powerfully associated with all cause mortality, adding further to the excess morbidity and mortality in the ESRD population [17,18].

In recent years, it has become increasingly apparent that the wasting syndromes attributed to PEW are not merely the result of undernutrition with reduced intake of protein and energy but may also involve other factors or conditions that reduce muscle mass or increase fat loss and/or energy expenditure. Based on new findings concerning syndromes of muscle wasting, malnutrition, and inflammation in individuals with acute kidney injury (AKI), or CKD, the International Society of Renal Nutrition and Metabolism (ISRNM) expert panel proposed in a 2008 report new terminologies and definitions related to wasting, cachexia, malnutrition, and inflammation [5].

The syndrome of protein-energy wasting (PEW) encompasses a number of nutritional and metabolic alterations which often coexist in patients with chronic kidney disease (CKD). These alterations result, collectively, in a progressive loss of body stores of protein and energy fuels (i.e., body muscle and fat mass).The consequences of PEW are many and important, with a negative impact on not only patients' prognosis, complications, management, and quality of life but also on health economics. [19,20].

Despite this evidence, PEW is often undetected and untreated, not being considered a clinical priority. Lack of awareness as well as insufficient knowledge and training are possibly major obstacles. Increased awareness of PEW in kidney disease starts by recognizing its prevalence along the CKD spectrum.

PEW prevalence in kidney disease patients is poorly defined till date. Reports often state wide and non-informative wide ranges such as 18-75%. Carrero et al. revealed that studies among AKI patients showed 60– 82% PEW prevalence, CKD 3–5 patients showed 11–54% PEW prevalence, and studies of transplant patients showed 28–52% PEW prevalence.

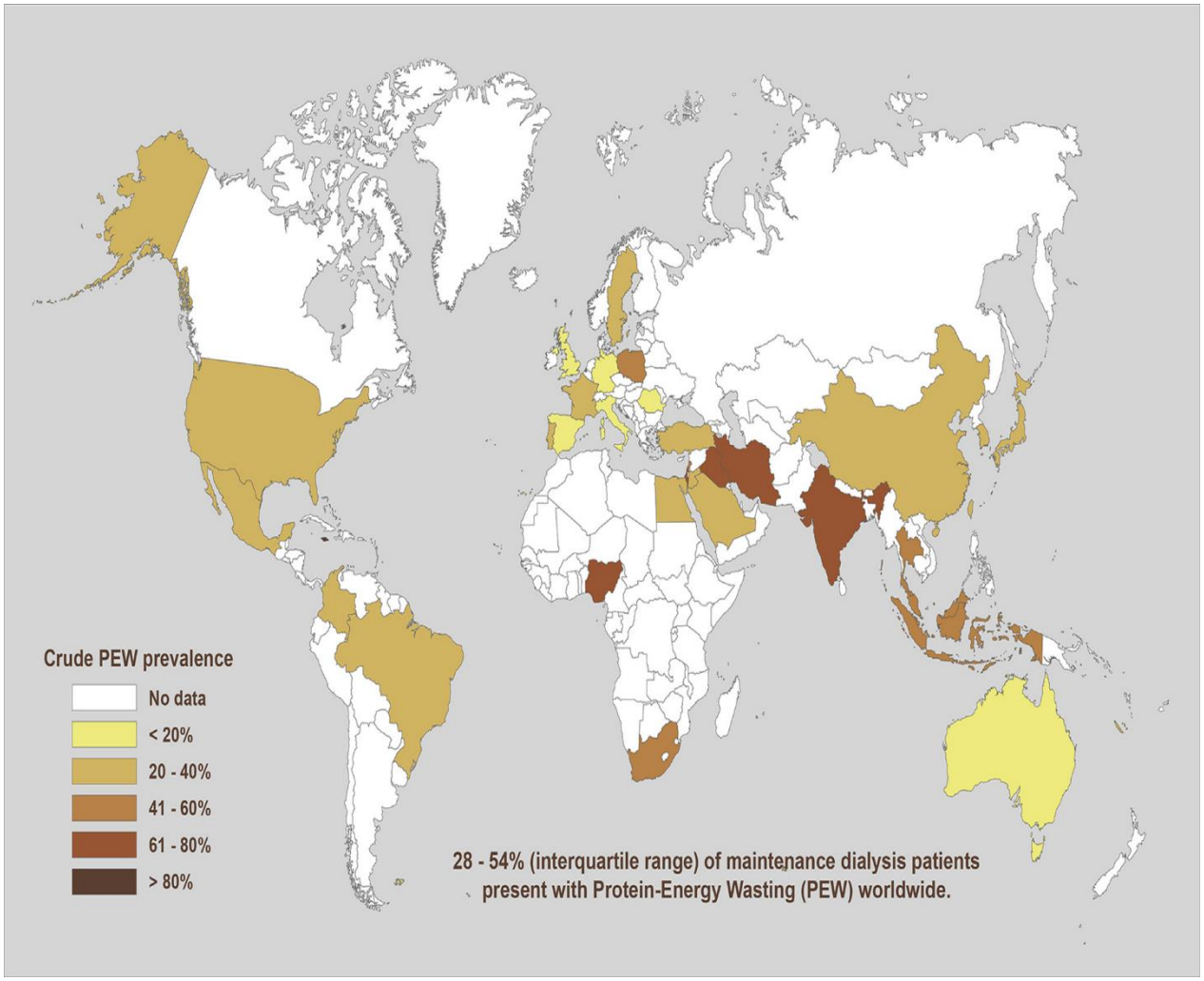


Fig no. 2 shows Prevalence of PEW among patients undergoing maintenance dialysis worldwide reported from studies published during 2000-2014. Color gradation reflects PEW prevalence in all included studies from each country (weighted averages within countries).

The evaluation of PEW prevalence from existing CKD literature is hampered by multiple factors, including lack of standardized PEW definitions, variability of existing assessment tools, studies with small sample size and differences in the socioeconomic realities of the countries in which the studies took place.

The International Society of Renal Nutrition and Metabolism (ISRNM) defines protein energy wasting as a "the state of decreased body stores of protein and energy fuels (that is, body protein and fat masses)" .This term was proposed by ISRNM in 2008 to specifically refer to a state of decreased body stores of protein and fat (wasting). This is to be distinguished from protein energy malnutrition (PEM),a form of protein energy wasting characterized purely by inadequate dietary intake. Moreover, unlike protein energy malnutrition, protein energy wasting cannot be corrected solely by increasing energy intake [21]

Clinical parameter	**Protein-energy malnutrition (PEM)**	**Protein-energy wasting (PEW)**
Pathogenesis	Explained by reduced nutrient and energy intake relative to metabolic demands of the body	Not completely explained by reduced nutrient and energy intake
Protein	Reduced	Reduced
Fat	May not be reduced	Reduced
Body Mass Index	May not be reduced	Reduced
Serum Albumin	May be reduced	Markedly reduced
Hypermetabolism	May be reduced	present
Hypercatabolism	May be reduced	present
Response to therapy	Condition improved by nutrient repletion	Condition not improved solely by nutrient repletion

Table no. 2 Comparison between protein energy malnutrition and Protein Energy Wasting.

The pathogenesis of protein energy wasting is complex and multifactorial. Decreased protein and energy intake due to anorexia, increased protein catabolism, decreased anabolism, chronic inflammation, metabolic acidosis and hormonal imbalances have all been linked to protein energy wasting as etiological factors.

PEW may be viewed as a complex heterogeneous disorder that results from an interplay of multiple

factors that directly or indirectly alter protein metabolism and energy balance. There are many causes of PEW in CKD, and these encompass a wide variety of conditions or disorders that ultimately leads to decreased protein and energy intake, increased protein loss or energy expenditure, or a combination of both factors as showing followings.

Causes of Protein-Energy Wasting in CKD/ESRD

1. Anorexia
2. Decreased nutrient intake
3. Endocrine disorders:
    - Insulin resistance
    - Decreased insulin-like growth factor-I
    - Hyperglucagonemia
    - Testosterone deficiency
    - Vitamin D deficiency
    - Hyperparathyroidism
4. Inflammation
5. Oxidative and carbonyl stress
6. Metabolic acidosis
7. Volume overload
8. Co-morbid conditions including diabetes and cardiac failure
9. Nutrient loss during dialysis treatment
10. Increased energy utilization
11. Abnormal protein kinetics

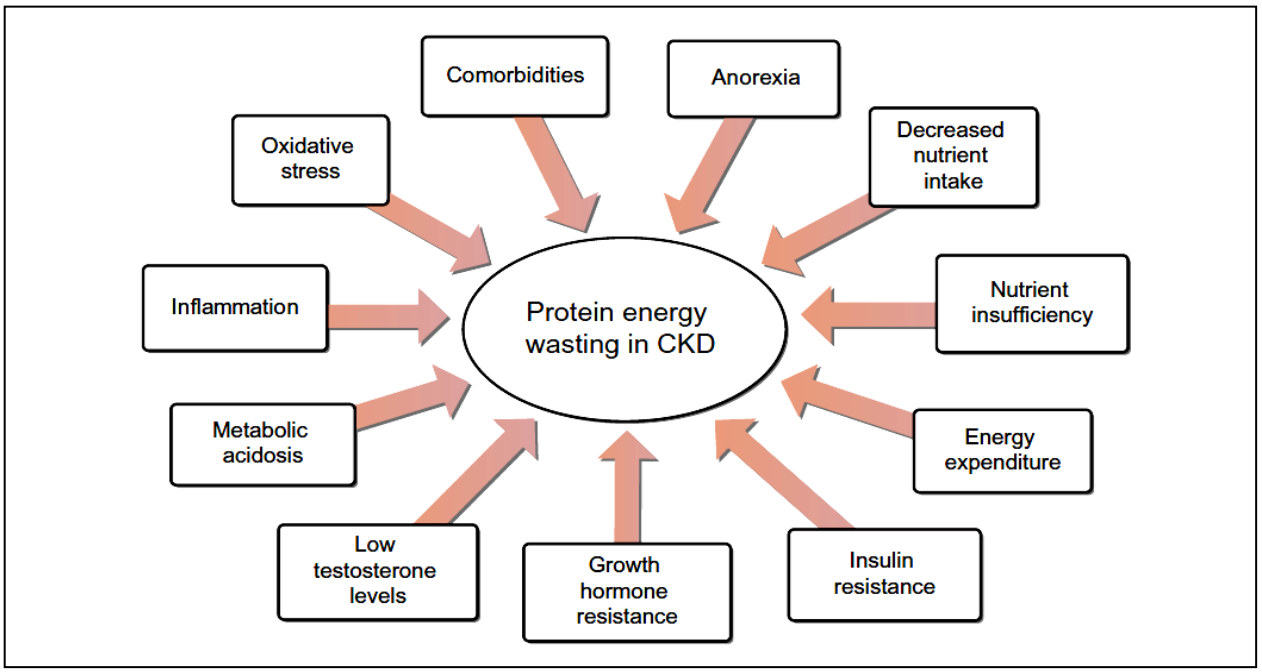


Fig. no. 3 shows Pathophysiology of Protein Energy Wasting (PEW) in CKD.

PATHOPHYSIOLOGY OF PEW IN CKD

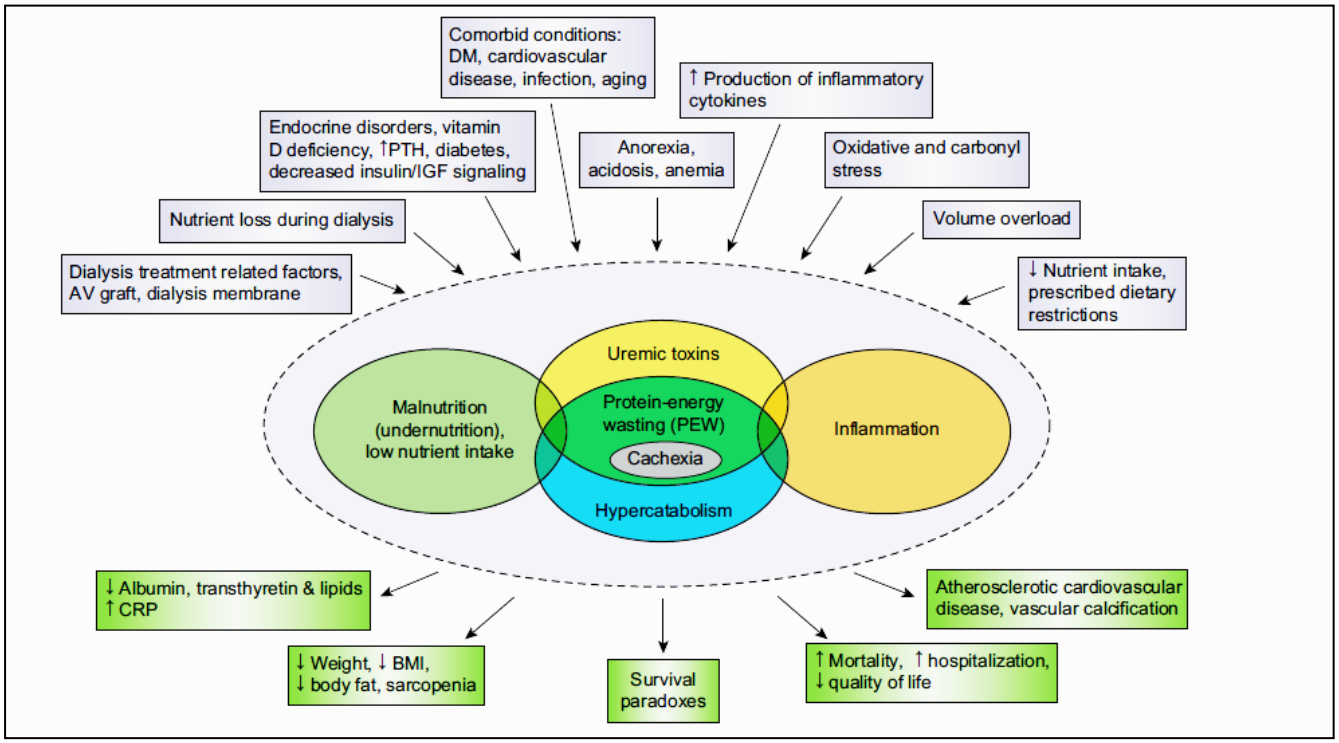


Fig no.4 representation of causes and manifestations of PEW in kidney disease

Anorexia

Anorexia is a cardinal manifestation of CKD. Several factors have been proposed to account for the anorexia associated with kidney disease. Evidence that uremic toxins can suppress appetite and food intake is derived from the studies of Anderstam and co-workers in experimental animals showing that intraperitoneal injection of uremic plasma ultrafiltrate into normal rats inhibits ingestion of nutrients. same group of investigators showed that intraperitoneal injection of a urine fraction or uremic plasma ultrafiltrate fraction inhibited carbohydrate intake by 76.3% and 45.9%, respectively [22]. An intracerebroventricular injection of 5 or 10 ml of urine middle molecule fraction (i.e., compounds with a molecular weight range of 300 to 2000 daltons) significantly inhibited carbohydrate intake. These data suggest that middle molecule compounds that accumulate in the plasma of uremic patients suppress food intake.

Decreased Nutrient Intake

Inadequate nutrient intake is considered the most important single cause of PEW in CKD and has been well documented in both adults and children with varying degrees of renal failure. The decline in dietary intake occurs early in CKD and accelerates as renal failure worsens. In children with CKD, low protein or energy intake due to anorexia is the primary reason for growth failure in this group. In a prospective study Ikizler [23] showed that spontaneous dietary protein intake (calculated from 24-h urine urea excretion) of patients with CKD significantly decreases as renal function declines. This decrease is most noticeable at creatinine clearance levels below 25 mL/min. In a large cohort of adult patients with moderate to advanced CKD, Kopple et al. showed that dietary protein intake and nutritional status correlated directly with the GFR. Especially, patients with a GFR of 21 mL/min/1.73 m2 or lower showed greater decline in nutritional status. Thus, dietary protein and calorie intake declines with decrease in GFR. The other factors that could contribute to decreased nutrient intake include depression, dementia and even economic barriers[24].

Impaired Gastric Motility

Several studies have documented an impairment of gastric motility in ESRD patients [25]. In one study more than 50% of nondiabetic ESRD patients who are receiving maintenance dialysis had abnormal gastric myoelectrical activity. Furthermore, administration of prokinetic agents to hypo albuminemic nondiabetic maintenance HD patients with occult gastroparesis was shown to improve gastric emptying, an effect that was accompanied by an increase in serum albumin [26].

The mechanism for the gastroparesis in ESRD patients is unclear, but it has been postulated that derangements in neuroendocrine signaling and imbalance in gut derived hormones may play a pathogenic role.

Gut-Derived Hormones

Apart from its well recognized digestive functions,the gut also produces peptides that have autocrine and paracrine as well as endocrine functions. These gut derived peptides maintain mucosal integrity, facilitate secretion of digestive enzymes, modulate gut motility and signal to the brain regarding the presence and absorptive status of nutrients; thus, they could play an important role in the genesis of PEW.

Ghrelin :- It is a unique hormone, principally secreted from the stomach. It acts to stimulate appetite and food intake via stimulation of the type 1a growth hormone secretagogue receptor [27]. Since ghrelin is a potent appetite-enhancer, it was initially thought that reduced levels of circulating ghrelin might be a potential mechanism for the reduced appetite seen in CKD. Surprisingly, plasma ghrelin was found to be elevated in patients with ESRD [28], and circulating ghrelin levels were found to be significantly higher in uremic patients with poor appetite when compared with uremic patients with good appetite. Recent studies have shown that exogenous administration of ghrelin improves appetite and/or increases food intake in animals and humans with CKD [29]. Thus, exogenous administration of ghrelin appears to be a promising strategy to improve food intake in malnourished ESRD patients.

Peptide YY(PYY):-It is another gut-derived hormone that plays an important role in the short-term regulation of appetite. This peptide is released by intestinal L cells in response to meals, suppresses appetite, and acts as a “break” to oral intake by complex mechanisms, which include vagal stimulation through interaction with the receptor Y2 (Y2R) of the hypothalamic arcuate nucleus. Increased plasma levels of PYY have been reported in patients with ESRD treated with dialysis, which could contribute to the anorexia and PEW of CKD [30].

Cholecystokinin (CCK):- It is an intestinal hormone known to cause early satiety and suppress appetite. It is released in response to eating and induces a state of satiety via peripheral and central receptors. Because circulating levels of CCK are increased in ESRD patients, it has been suggested CCK may contribute to the premature satiety and anorexia in CKD.

Insulin and Insulin-Like Growth Factors (IGF)

The most common and important endocrine disorder in CKD is the development of insulin

resistance [31]. Insulin is a potent anabolic hormone; even a small increase in plasma insulin stimulates protein synthesis and exerts a powerful inhibitory effect on protein catabolism. Resistance to the actions of insulin has been shown to be strongly associated with increased muscle breakdown in non-diabetic chronic HD patients [32].

Insulin-like growth factor-I:- (IGF-I), which has a 48% amino acid sequence identity with proinsulin, enhances insulin sensitivity and independently stimulates protein synthesis and suppresses protein degradation in both experimental animals and human subjects. Kopple and associates showed that mRNA levels of IGF-IEa, IGF-II, and the IGF-I receptor are decreased in the skeletal muscle of ESRD patients. There is an attenuation in the IGF-I-induced stimulation of protein synthesis and inhibition of protein degradation in skeletal muscle in CKD [33]. Among the known mechanisms for IGF-I resistance in CKD are defects in the phosphorylation and activity of the intrinsic tyrosine kinase of the IGF-I receptor and plasma inhibitors of IGF-I and elevated basal cytosolic [Ca2þ].Bailey et al.have shown that CKD causes defects in IGF-I signaling in skeletal muscle, an effect that is associated with a decrease in phosphorylation of Akt and an increase in proteolysis and muscle wasting. Another mechanism closely linked to impaired IGF-I signaling in CKD is dysfunction of skeletal muscle precursors or satellite cells, which are responsible for maintaining muscle growth and repair [34].

Interestingly, administration of thiazolidinedione (TZD) in a rodent model of insulin resistance improved insulin resistance and decreased protein degradation in muscle.

Furthermore, in a recent clinical study of a large cohort of incident HD patients with diabetes, non-insulin requiring type-2 diabetic subjects receiving TZDs had significantly higher body mass indices, and serum albumin levels, than those not receiving TZDs [35]. Prospective studies are needed to confirm these findings and to explore the potential beneficial role of insulin sensitizers in the treatment of ESRD patients with or at risk for PEW.

Resistance to Growth Hormone

Growth hormone (GH) regulates muscle and fat metabolism, which impacts on body composition and insulin sensitivity. Decreased or impaired action of growth hormone is another endocrine disturbance associated with CKD that may retard muscle growth and promote muscle protein catabolism. Insensitivity to GH is the consequence of multiple defects in the GH/IGF-I signalling. GH activation of the Janus kinase 2-signal transducer (JAK2) and activator of transcription (STAT) signal transduction pathway is depressed in advanced CKD, and this leads to reduced IGF-I expression

and resistance to IGF-I [36]. However, administration of GH has been shown to increase linear growth in children with CKD and improve net protein balance in malnourished adult ESRD patients on maintenance HD.

Pupim et al. showed that short-term rhGH therapy (for three consecutive days) in chronic HD patients resulted in a significant accrual of whole body protein mass, primarily through an 18% increase in whole-body protein synthesis associated with a reduction essential amino acid muscle loss.

Finally, GH treatment in ESRD patients resulted in increased lean body mass and improved quality of life as well as decreased cardiovascular risk [37].

Testosterone Deficiency

Testosterone regulates many physiological processes, including sexual function, muscle protein metabolism, cognitive functions, erythropoiesis, plasma lipids, and bone mineral metabolism. More than 60% of men with advanced CKD have low plasma concentrations of testosterone, and this is associated with increased mortality [38]. Macdonald JH et al showed that treatment with nandrolone decanoate for 24 weeks, produced a two-fold increase in appendicular lean mass in patients with CKD.

Potential mechanisms by which testosterone deficiency might cause muscle catabolism include altered IGF-I signaling and an increase in myostatin, a protein that suppresses muscle growth.

Altered Adipokine Physiology

Adipose tissue has traditionally been viewed as a passive reservoir for storage of energy. However, in recent years it has emerged as a highly active endocrine organ that secretes a variety of bioactive peptides, known as adipokines, which mediate numerous biological and pathological processes including energy metabolism, neuroendocrine function, sex steroid metabolism, and immune function. The underlying mechanisms whereby endocrine hormones and adipokines cause anorexia and decreased nutrient intake in CKD are complex and may involve the participation of neuroendocrine pathways that control food intake and energy homeostasis (Figure 11.2).

Leptin, the protein product of the ob-gene, is secreted by adipocytes and acts as a lipostat mechanism to regulate food intake and energy expenditure via modulation of satiety signals in the hypothalamus. An increase in the level of leptin decreases neuropeptide Y, reduces food intake, increases energy expenditure, induces weight loss, lowers plasma insulin, alters glucose homeostasis and induces muscle protein breakdown. Serum leptin concentrations are elevated in CKD patients who do not have ESRD [39].

Longitudinal studies have also shown that increased serum leptin levels are associated with weight loss in dialysis patients [40].

Adiponectin is another adipocyte-derived hormone that has been shown to modulate food intake and energy homeostasis. In addition, adiponectin has insulin sensitizing, anti-atherogenic, and anti-inflammatory properties. Data regarding the role of adiponectin in PEW in CKD are limited. Despite the high prevalence of insulin resistance in CKD, circulating levels of adiponectin are increased among patients with CKD [41].

Effect Of Volume Overload

Chronic volume overload and concomitant heart failure are frequent complications of CKD. There is increasing evidence that fluid volume overload may contribute to malnutrition in CKD patients that may contribute to PEW. For instance, volume overload is associated with inadequate dietary protein and energy intake and nutritional status in maintenance PD patients [42]. In a large cohort of ESRD patients undergoing renal replacement therapy, plasma levels of the N-terminal fragment of B-type natriuretic peptide (NT pro-BNP) and the extracellular fluid volume/total body water (ECFv/TBW) ratio were correlated with several markers of inflammation and poor nutrition [43]

These data suggest that there may be a link between the malnutrition-inflammatory state and hypervolemia in patients with CKD.

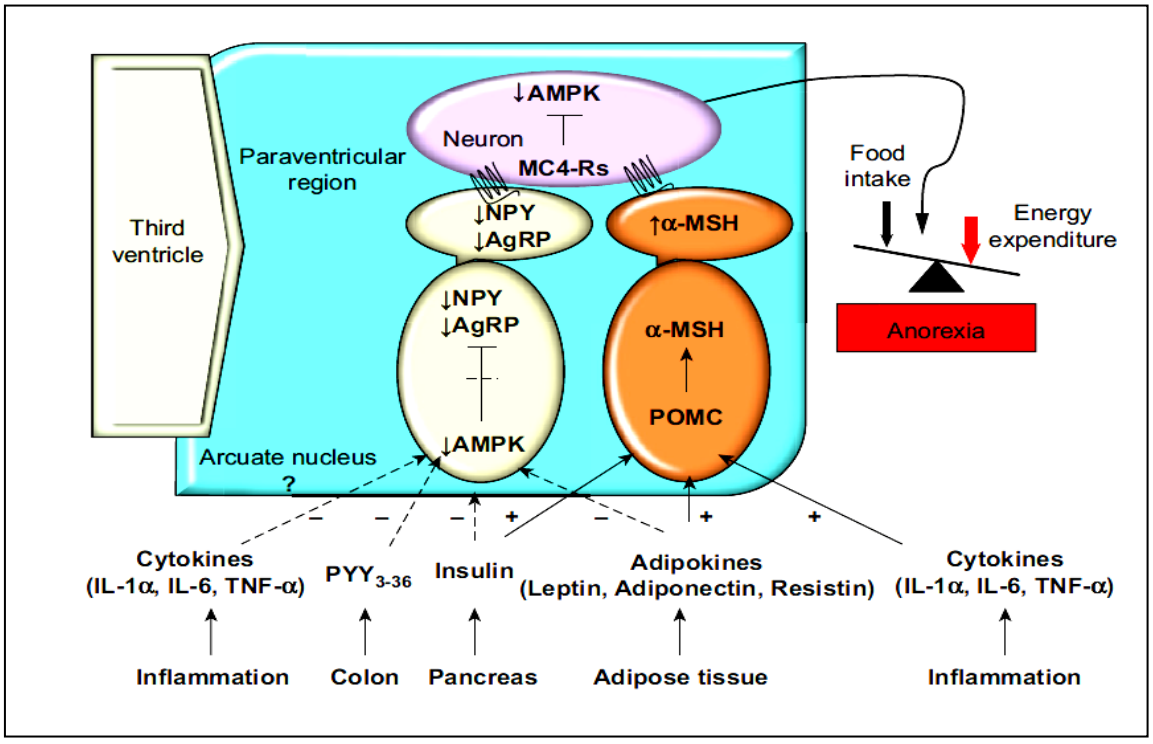


Fig. no.5 Orexigenic and anorexigenic mechanisms controlling energy homeostasis in CKD

Role Of Metabolic Acidemia

The National Kidney Foundation Kidney Disease and Dialysis Outcome Quality Initiative guidelines to maintain a serum bicarbonate level in ESRD patients of at least 22 mEq/L. Accordingly, Kalantar-Zadeh and associates observed that a serum bicarbonate level of >22 mEq/L had lower death risk among ESRD patients [44]. Catabolic effects of metabolic acidemia may result from an increased activity of the adenosine triphosphate (ATP)-dependent ubiquitin-proteasome and branched-chain amino acid oxidation.

A recent clinical trial showed that bicarbonate supplementation in patient with CKD not only improved their nutritional status but also slowed progression of the renal disease [45].

In a randomized, cross-over metabolic balance study of eight end stage renal disease patients treated with peritoneal dialysis, increasing the arterial pH from 7.38 to 7.44 resulted in significantly higher net positive nitrogen balances in all but one patient [46].

INFLAMMATION: -Agent Provocateur Of PEW

A large body of evidence indicates that inflammation plays a central role in the pathogenesis of PEW in CKD beyond its role in protein catabolism. For example, cytokines, such as tumor necrosis factor (TNF)-a, interleukin (IL)-1, and IL-6, can cause anorexia by acting on the central nervous system via modulation of the melanocortin signaling system to alter the release and function of several key neurotransmitters that regulate appetite and metabolic rate (Figure 11.3).

It is becoming increasingly clear that intra-dialytic loss of amino acids, and the resultant deficiency of amino acids is only a part of the paradigm, the other being cytokine activation facilitating augmented protein catabolism [47].

Furthermore, studies showed IL-6 leads to activation of genes promoting protein catabolism, efflux of amino acids from the muscle and increased synthesis of hepatic acute phase proteins during HD.

The same group of investigators observed that caspase-3 activity in the skeletal muscle, accumulation of 14 kDa actin fragment (a measure of muscle protein breakdown) and apoptosis are increased during HD [48]. Muscle protein catabolism was positively associated with caspase-3 activity and skeletal muscle IL-6 content.

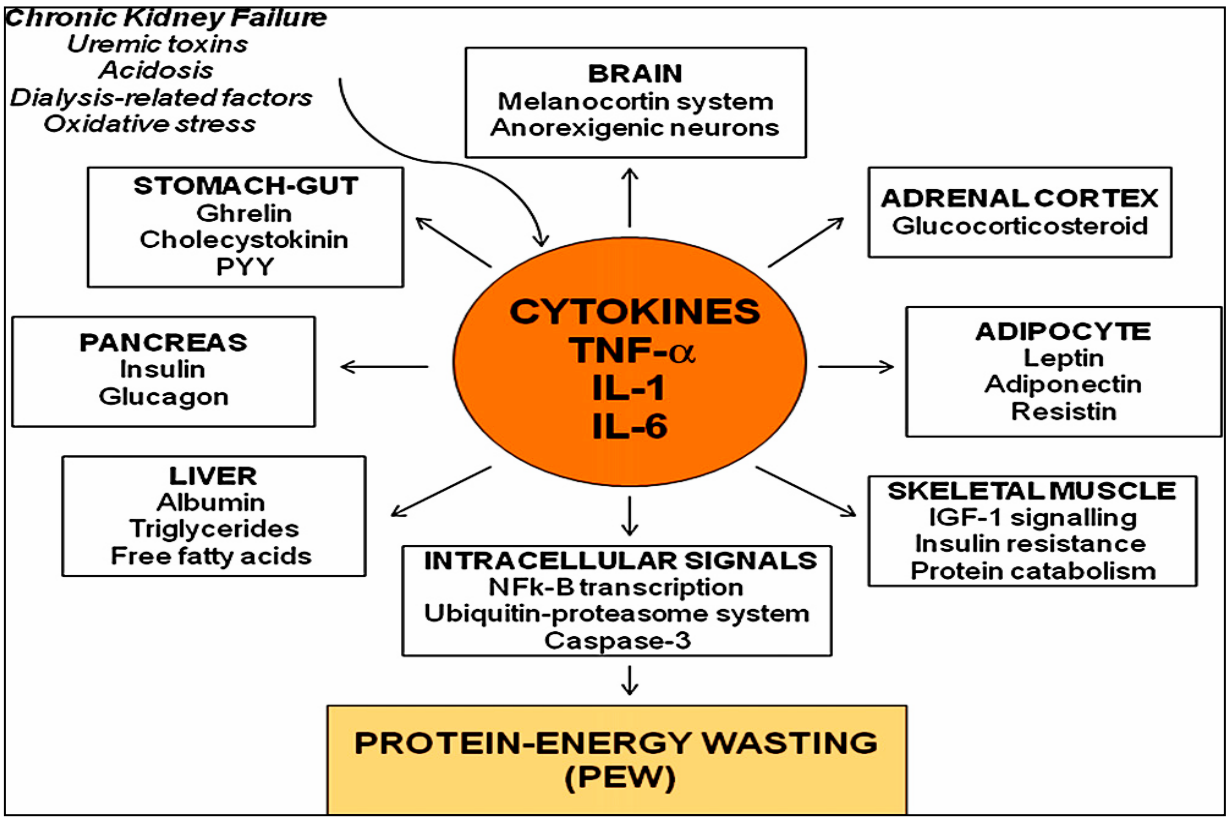


Fig no. 6 Central role of cytokines in the pathophysiology of protein energy wasting in CKD.

OXIDATIVE STRESS: - Other Key Pathways

CKD is characterized by activation of renin angiotensin system. Interestingly, angiotensin II infusion has been shown to induce skeletal muscle atrophy, which was associated with oxidative stress, increased expression of the E3 ligases atrogin-1/MuRF-1 and augmented ubiquitin-proteasome mediated proteolysis [49].

Nuclear factor-kB (NF-kB) is at the interface between oxidative stress and inflammation and is activated during haemodialysis [50]. NF-kB inhibits myogenesis by promoting myoblast growth and inducing loss of MyoD, which stimulates skeletal muscle differentiation and repair. Another molecule, myostatin, a member of the transforming growth factor-b superfamily of signal transduction proteins is an important regulator of skeletal muscle mass and repair.

ALTERED PROTEIN KINETICS IN CKD

An increase in net proteolysis due to imbalance between protein synthesis and degradation has been reported in uremic animals [51]. The results from the human studies, however are more controversial than those from animal studies. Muscle and whole body protein turnover studies in stable advanced CKD/ ESRD patients have consistently shown that there is a balanced reduction in protein synthesis and degradation, such that there is no net protein loss.

Ikizler found that protein catabolism is increased during HD, with no significant change in protein synthesis. Using multiple tracers, Raj et al. observed a significant increase in both protein synthesis and breakdown during HD.

Albumin is a negative acute phase-protein, and fibrinogen is a positive acute-phase protein. In healthy humans, albumin and fibrinogen account for ~50 and ~10% of the total liver protein synthesis, respectively. The change in albumin, fibrinogen and muscle protein synthesis rates vary according to the pathophysiological state.

Peritoneal dialysis treatment provides 300 to 600 kcal/daye1 primarily from absorption of glucose from the use of dextrose-based dialysis solutions resulting in hyperinsulinemia in these patients. Goodship et al. performed leucine turnover studies in CKD patients before and after three months of continuous ambulatory PD (CAPD) treatment. They observed that protein turnover is decreased at baseline, but the balance between synthesis and breakdown is higher and remained unchanged after three months on CAPD. Long term use of amino acid based PD fluid has been shown to induce a positive protein balance [52]. About 80% of leucine contained in the dialysate solution is absorbed through peritoneum and about 43% of the leucine absorbed is used for protein synthesis.

DIAGNOSIS OF PEW IN CKD

The guidelines for diagnosis of PEW by the International Society of Renal Nutrition and Metabolism (ISRNM) establish standard nomenclature and definitions for PEW in CKD.

Diagnosis of PEW in CKD patients is determined by four key categories:

1) Changes in biochemical indicators,
2) Weight loss, decrease in total body fat, and low body weight,
3) Decrease in muscle mass
4) Low protein or energy intake

Readily utilizable criteria for the clinical diagnosis of PEW in CKD [21].

Serum Chemistry

- Serum albumin <3.8 g/dL[a]
- Serum prealbumin (transthyretin) <30 mg/dL (for maintenance dialysis patients only)[a]
- Serum cholesterol <100 mg/dL[a]

Body mass

- Body mass index (edema free) <23[b]
- Unintentional weight loss over time: 5% over 3 months or 10% over 6 months
- Total body fat percentage <10%

Muscle Mass

- Reduced muscle mass 5% over 3 months or 10 over 6 months
- Reduced mid-arm muscle circumference area[c] (reduction >10% in relation to 50th percentile of reference population)
- Creatinine appearance[d]

Dietary intake

- Unintentional low DPI <0.80 g/kg/day for at least 2 months for dialysis patients or <0.6 g/kg/day for patients with CKD stages 2–5
- Unintentional low DEI <25 kcal/kg/day for at least 2 months

≥3 out of the 4 listed categories along with at least one test in each of the selected category must be satisfied for the diagnosis of kidney disease-related PEW. Each criterion should be documented on at least three occasions, preferably 2–4 weeks apart.

[a]Not valid in abnormally great urinary or gastrointestinal protein losses, liver disease, or cholesterol-lowering medicines;

[b]A lower body mass index might be favourable in certain Asian populations;

[c]Measured by a trained anthropometrist;

[d]Creatinine appearance is influenced by both muscle mass and meat intake.

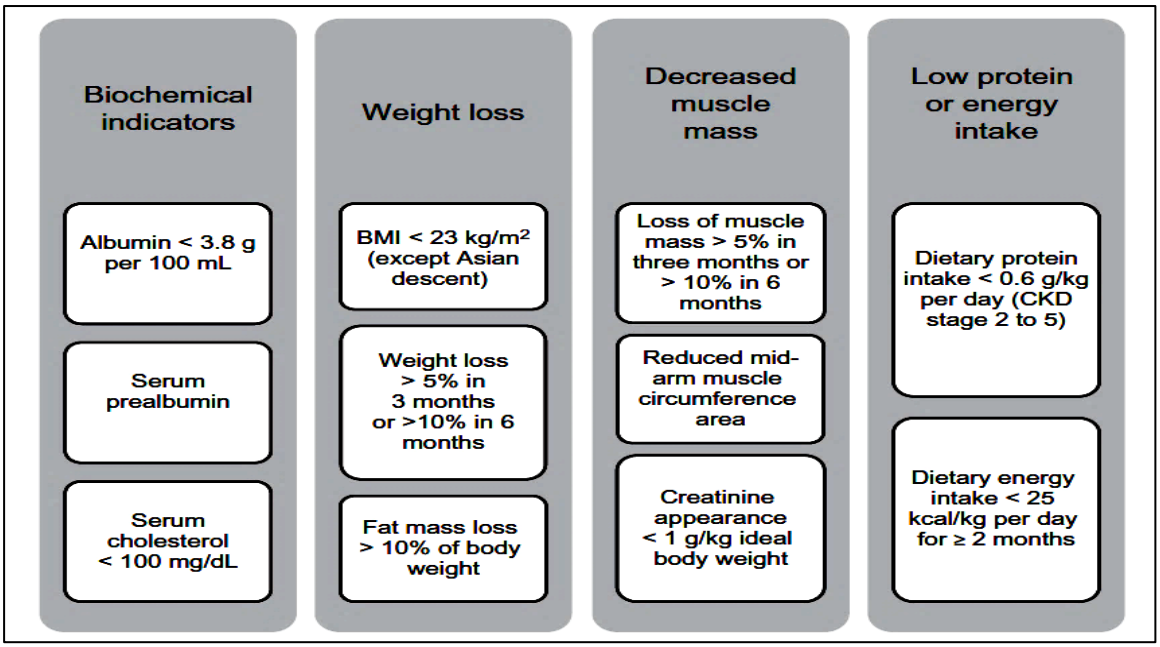


Fig no. 07 shows ISRNM Diagnostic criteria of PEW

The ISRNM also identified several other measures of body composition, laboratory markers, nutritional scoring systems, and food intake and expenditure that are recognized as important indicators, but not diagnostic tools, for PEW. Measures of body composition that are used to measure body fat and muscle mass include CT or MRI of muscle mass, energy beaming technologies (DEXA, NIR, BIA), air or underwater displacement weighing, muscle measures (muscle fiber size, proportion of muscle fiber types, muscle alkaline soluble protein, and the 14 kDa fragment of actomyosin), total body nitrogen and total body potassium.,53The 14 kDa actomyosin fragment serves as a strong indicator of muscle breakdown, and levels have been shown to be elevated in catabolic states, such as ESRD. [53] In patients with ESRD, the amount of the fragment increases before HD treatment and is further elevated after completion of dialysis. Laboratory measures can also be used as indicators of PEW, including urea, triglycerides and IGF-1.

Nutrition Markers	NKF KDOQI 2000	ESPEN 2009	ISRNM 2013
Laboratory	Albumin < 4.0 g/dL	Albumin <35 g/L Transthyretin <300mg/L	Albumin <3.8 g/dL Prealbumin <30 mg/dL Serum cholesterol <100mg per 100 ml
Body fat mass and weight	>6% edema-free usual BW loss or <90% of IBW in <6 months	BMI <20kg/m2 Loss of BW ≥10% in 6 months	BMI <23 Unintentional weight loss over time: 5% over 3 months or 10% over 6 months Total body fat percentage <10%
Dietary Intake	DPI <1.0g/kg/d	NR	DPI <0.8g/kg/d for at least 2 months DEI < 25 Kcal/kg/d for at least 2 months
Anthropometry	NR	NR	Reduced muscle mass 5% over 3 months or 10% over 6 months Reduced MAMC area (reduction >10% inrelation to 50th percentile of reference population)
Nutrition Assessment	SGA malnourished	NR	NR
Appetite	Poor appetite/poor oral intake	NR	NR

Table no. 03 Diagnostic Criteria for Protein Energy Wasting (PEW) in Malnourished Chronic Kidney Disease Patients.

Other potential tools for assessment of PEW in individuals with CKD stages 3–5

- Appetite, food intake, and energy expenditure
  - appetite assessment questionnaires
  - population-based dietary assessments: food frequency questionnaires
  - measuring energy expenditure by indirect or direct calorimetry

- Body mass and composition
  - weight-based measures: weight-for-height
  - total body nitrogen
  - total body potassium
  - energy-beam-based methods: DEXA, NIR, BIA, and vector bioimpedance analysis
  - underwater weighing and air displacement weighing
  - 14 kDa fragment of actomyosin
  - microarrays
  - muscle fiber size
  - relative proportions of muscle fiber types
  - muscle alkaline soluble protein
  - CT and/or MRI of muscle mass

- Laboratory markers
    - serum biochemistry: transferrin, urea, triglyceride, bicarbonate
    - hormones: leptin, ghrelin, growth hormones
    - inflammatory markers: CRP, IL-6, TNF-α, IL-1, SAA
    - peripheral blood cell count: lymphocyte count or percentage
    -
- Nutritional scoring systems which are mentioned below

Subjective Global Assessment Score (SGA)

Nutrient intake, weight change, symptoms (abdominal pain, dental pain, anorexia, early satiety, nausea, vomiting, constipation, dysphagia, diarrhea). Functional capacity, metabolic requirements, physical exam findings. These go into calculating final SGA rating.

MIS/KALANTAR score

Change in dry weight, dietary intake, gastrointestinal symptoms, functional capacity, comorbidity, change in fat stores, signs of muscle wasting, BMI (kg/m2), serum albumin (g/L), serum total iron-binding capacity (mg/dL). Scored 0–3 (0 not present, 3 is severe)

GNRI

The GNRI was calculated from the patient's serum albumin and body weight by using the equation developed by Bouillanne et al. by modifying the nutritional risk index for elderly patients as follows:

GNRI= [14.89 X albumin (g/dl)] + [41.7 x (body weight/ideal body weight)]

Assessments of physical function for CKD patients with malnutrition

- Muscle strength
    - Knee Extension Strength (Isometric or Isokinetic)
    - Handgrip strength
    - 5-chair stand
- Gait ability
    - Gait speed
- Balance function
    - One-leg stand
    - Timed Up and Go Test
- Berg Balance Scale

- Muscle mass
    - Bioelectrical impedance analysis (BIA)
    - Dual-energy X-ray absorptiometry (DXA)
    - Mid-arm muscle circumference (MAMC)
    - Calf circumstances (CC)
    - Creatinine index (CI)

- Exercise capacity
    - Cardiopulmonary Exercise testing (CPX, CPET or CPEX)
    - 6-min walk distabce/test (6MWD/6MWT)
    - 400-meter walk test
- General physical performance
    - Short Physical Performance Battery (SPPB)
    - SARC-F
- SARC-CalF

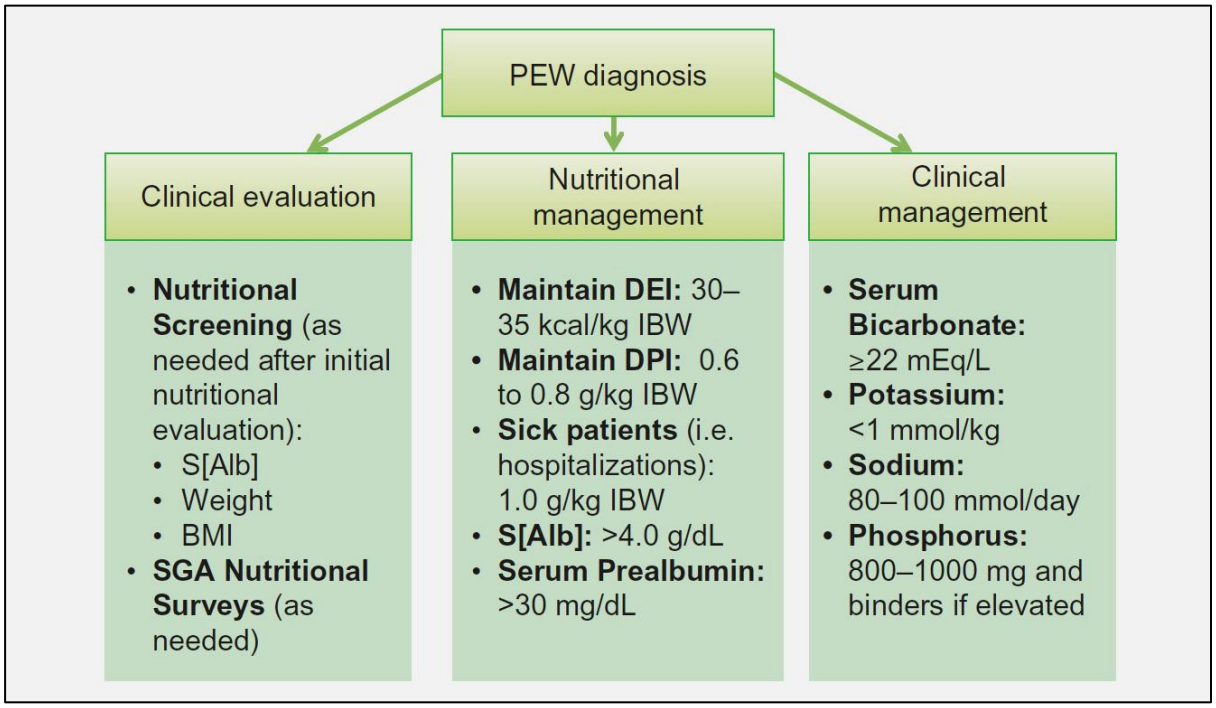


Fig no. 08 Recommendations and guidelines for treatment of patients with PEW in CKD

Table no.04 Represents different treatment options in CKD

Nutrient Insufficiency	Low protein diet and nutritional supplements Keto-analogue supplements	Suplena (low protein/high caloric) supplement slows progression of CKD and improves nutritional parameters Sustains kidney function and maintains serum albumin and total protein levels	Montes-Delgado et al. 1998 Prakash et al. 2004, Kalanter-Zadeh et al. 2011
Growth Hormone Resistance	Recombinant human growth hormone Super-agonist of human GHRH (AKL-0707)	Increases growth rate and catch-up growth to almost normal height (1.6 ± 1.2 SD below normal Increases fat mass and decreases serum urea	Fine et al. 1994,Haffner et al. 2000 Niemczyk et al. 2010
Low Testosterone	Nandrolone decanoate injections	Increases percentage of lean body mass	Eiam-Ong et al. 2007
Metabolic Acidosis	Oral bicarbonate	Increases lean body mass, improves dietary protein intake, and slows progression of CKD to ESRD	de Brito-Ashurst et al. 2009
Muscle Biology Dysfunction	Resistance exercise	Increases muscle mass and mitochondrial DNA copy number; increases muscle strength and protein utilization; lowers inflammation	Balakrishnan et al. 2010,Castaneda et al. 2004
Inflammation	Pentoxifylline infusion	Decreases whole body proteolysis	Biolo et al. 2002

Obesity Paradox in End-Stage Kidney Disease Patients

In the general population, obesity is associated with increased cardiovascular risk and decreased survival. In patients with end-stage renal disease (ESRD), however, an "obesity paradox" or "reverse epidemiology" (to include lipid and hypertension paradoxes) has been consistently reported, i.e. a higher body mass index (BMI) is paradoxically associated with better survival.

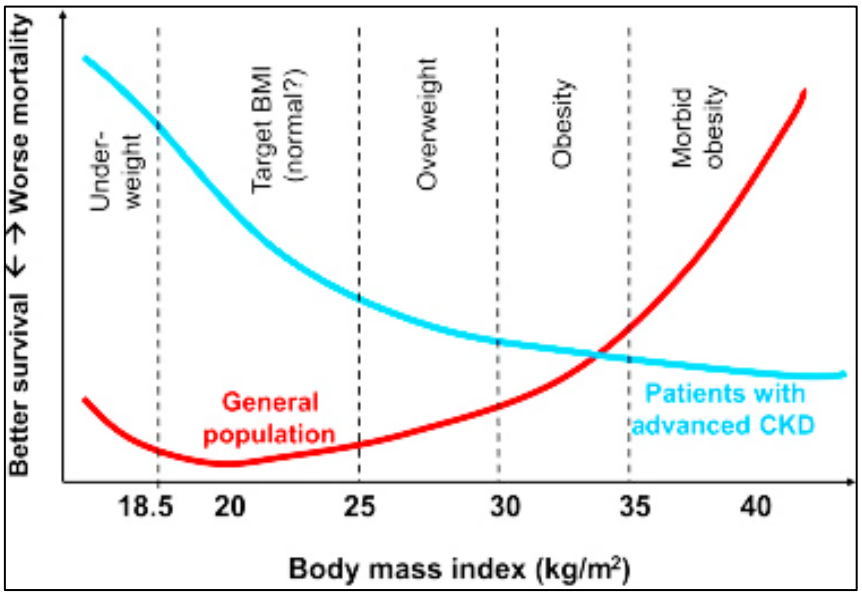


Fig no.09 Represent reverse association of body mass index (BMI) and survival in patients with CKD.

Potential mechanisms in Obesity paradox:-

- Kidney Disease Wasting (Malnutrition–inflammation complex syndrome)
- Time discrepancy between competitive risk factors: over-nutrition vs. undernutrition
- Unusual genetic constellation due to survival selection during CKD progression
- Sequestration/storage of uremic toxins in fat tissue
- Anti-inflammatory cytokines related to body mass, including adiponectin
- Tumor necrosis factor alpha receptors
- Endotoxin-lipoprotein hypothesis
- Stability of hemodynamic status in obese patients
- Neuro-hormonal alterations in obesity

- Alteration of conventional risk factors in uremic milieu ('beyond Framingham')
- Survival bias
- Reverse causation

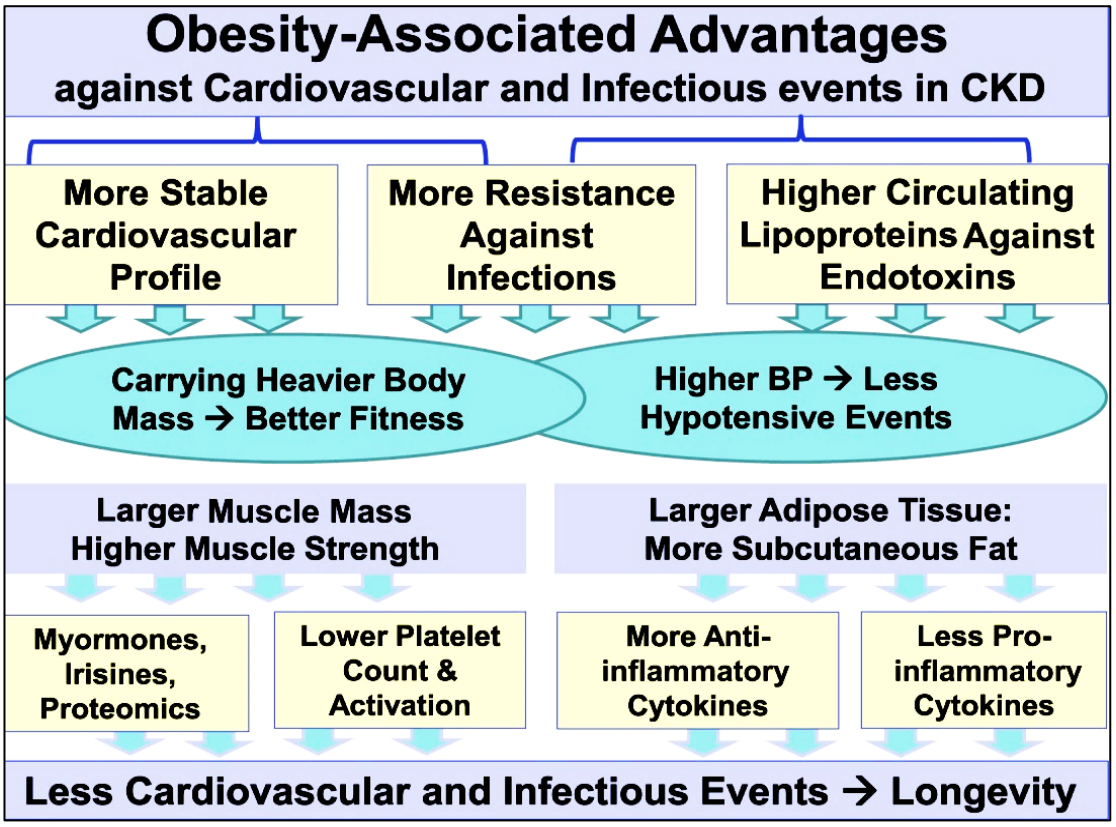


Fig no. 10 Shows Putative mechanisms of obesity paradox in chronic kidney disease (CKD)

Most studies have shown that the inverse association between BMI and mortality in HD patients is independent of demographics, co-morbidities and other nutritional markers, although because of methodological differences, only limited comparisons can be made. Important epidemiologic studies are summarized in Table given below. These clinical studies all take into account the clinical characteristics of the patients.

STUDY	PATIENTS	RESULT
Degoulet, et al. [54] 1982	**1435 HD**	**Lower BMI (<20 kg/m2) was associated with higher over-all and CV mortality**
Fleischmann, et al. [55] 1999	1346 HD	Better survival with overweight and obesity.
Kopple et al. [56] 1999	12965 HD	Lowest mortality rates in overweight MHD patients.
Wolfe et al. [57] 2000	9165 HD	Better survival in overweight and obese MHD patients. USRDS data.
Leavey et al. [58] 2001	9417 HD	Mortality risk decreased with increasing BMI in both US and European MHD patients in the DOPPS
Port et al. [59] 2002	45967 HD	The highest BMI tertile had the lowest mortality risk. Data from the US Federal billing records
Lowrie et al. [60] 2002	433334 HD	The log of risk decreased linearly for weight, weight-for-height, and BSA and was reverse J-shaped for weight/height and BMI
Glanton et al. [61] 2003	151027 HD & PD	Obesity defined as BMI ≥30 kg/m2 was associated with reduced mortality, which was stronger in African Americans.
Johansen et al. [62] 2004	418055 HD & PD	High BMI, adiposity, and fat mass were associated with increased survival in all but Asian Americans
Kalantar et al. [63] 2005	54534	Time-varying BMI and weight gain over time were associated with improved cardiovascular mortality
Kalantar-Zadeh et al. [64] 2012	121,762 HD	Lower BMI, lower muscle mass, weight and muscle loss over time were associated with higher death rates. In joint effect analysis, a decline in muscle mass estimated with serum creatinine appeared to be a stronger predictor of mortality than did weight loss
Park et al. [65] 2013	40,818 HD	Mortality risks were lower across higher BMI, which was identical among Asian vs. white and African Americans.

Table no. 05 Represent Summary of studies with large sample size (>1000 subjects) evaluating the association between BMI and outcomes in HD patients.

PREVALENCE OF LOW PHYSICAL FUNCTION, FRAILTY, AND SARCOPENIA IN CHRONIC KIDNEY DISEASE:-

Low physical function and frailty have been recognized as major complications in ESRD patients receiving dialysis. In the dialysis population, levels of physical function, as defined by leg muscle strength, walking speed, balance function, and range of motion, have been found to be approximately 60–70% of that of healthy persons without CKD Additionally, sarcopenia, which refers to low muscle mass and reduced skeletal muscle strength, as ascertained by reduced handgrip strength and/or low gait speed, is frequently observed in dialysis patients. The prevalence of sarcopenia among maintenance haemodialysis (MHD) and CPD patients, as defined by the European Working Group on Sarcopenia in Older People (EWGSOP) and the Asian Working Group for Sarcopenia (AWGS) criteria, ranges from 12.7 to 40.0% and 8.4 to 11.0%, respectively. Studies related to prevalence of sarcopenia, frailty in CKD & ESRD are mentioned in the tables below.

STUDY	Study Population: Mean age, % sex, mean eGFR	Physical Function Outcome	Prevalence
Pereira RA, et al. [66] 2015 Brazil	287 CKD patients (Stage 3–5) Age 59.9 ±10.5 Male 62% eGFR 25.0 ± 15.8	Sarcopenia defined by ① Handgrip strength ± Mid-arm muscle circumference ② Handgrip strength ± Subjective global assessment ③ Handgrip strength ± Skeletal Muscle Index	Sarcopenia ① 9.8% ② 9.4% ③ 5.9%
Zhou Y, et al. [67] 2018 Sweden	148 CKD patients (Stage 3–5) Age 66 Male 66.2% eGFR 22.5 ± 8.2	Sarcopenia defined by EWGSOP criteria	Sarcopenia 14%
Souza VA, et al. 2017 Brazil	100 CKD patients (Stage 2–5) Age 73.59 ± 9.22 Male 41% eGFR 35.96 ± 16.01	Sarcopenia defined by EWGSOP and FNIH criteria	Sarcopenia (EWGOP) 11.9% (FNIH) 28.7%
D'Alessandro C, et al. 2018 Italy	80 CKD patients (Stage 3b-4) Age 73.7 ± 7.2 Male 100% eGFR 28.3 ± 9.8	Sarcopenia defined by EWGSOP criteria	Sarcopenia (60–74 years old) 12.5% (> 75 years old) 55.0%
Ishikawa S, et al. 2018 Japan	260 CKD patients (Stage 3–5) Age 76.0 (69.0–80.0) Male 65% eGFR 31.5 ± 12.9	Sarcopenia defined by AWGS Criteria	Sarcopenia 25.0%

Lee SJ, et al. [68] 2015	168 CKD patients (Stage 2–4) (Frailty population) Age 69.5 ± 13.9 Male 55.6% eGFR 38.7_14.1 (non-Frailty population) Age 63.7 ± 13.5 Male 67.6% eGFR 42.6 ± 16.8	Frailty defined by modified CHS criteria	Frailty 37.5%
Walker SR, et al. 2015 Canada	217 CKD patients (Stage 4–5) Age 70.3 (60.0 – 79.1) Male 60% eGFR 19 (14–27)	Frailty (Short physical performance battery < 10)	Frailty 56% Frailty 37.5%
Reese PP, et al. 2013 USA	1111 CKD patients with eGFR 20- 70 Age 65 (57–71) Male 53%	Frailty defined by modified CHS criteria	Frailty 7% Pre-Frailty 43%
Roshanravan B, et al. [69] 2012 USA	336 CKD patients (Stage 1–4) Age 58.7 ± 13.0 Male 81% eGFRcys 50.9 ± 27.1	Frailty defined by modified CHS	Frailty eGFRcys _ 60: 8.1% 45–59: 8.1% 30–44: 21.6% < 30: 18.7%

Table no. 06 Epidemiologic studies of the prevalence of physical function, frailty, and sarcopenia in CKD

Table no. 07 Epidemiologic studies of the prevalence of physical function, frailty and sarcopenia in ESRD

Isoyama N, et al. [70] 2014 Sweden	330 incident dialysis patients Age 53 ± 13 Male 61.5%	Sarcopenia defined by EWGSOP criteria	Sarcopenia 20%
Kim JK, et al. [71] 2014 Korea	95 haemodialysis patients Age 63.9 ± 10.0 Male 57.2%	Sarcopenia defined by EWGSOP criteria	Sarcopenia 33.7%
Ren H, et al. [72] 2016 China	131 haemodialysis patients Age 49.4 ± 11.7 Male 61.1%	Sarcopenia defined by EWGSOP criteria	Sarcopenia 13.7%
Bataille S, et al. [73] 2017 France	111 haemodialysis patients Age 77.5 (70.8–84.8) Male 58.6%	Sarcopenia defined by EWGSOP criteria	Sarcopenia 31.5% Low muscle strength 88.3% Low muscle mass 33.3%
Marini ACB, et al. [74] 2020 Brazil	95 haemodialysis patients (With sarcopenia risk population) Age 64.9 ± 13.9 Male 42.9% (Without sarcopenia risk population) Age 56.9 ± 14.6 Male 67.6%	Sarcopenia risk (SARC-F _ 4	Sarcopenia risk 22%

Lin YL, et al. [75] 2020 Taiwan	126 haemodialysis patients Age 63.2 ± 13.0 Male 51.6%	Sarcopenia defined by Taiwan criteria and EWGSOP criteria	Sarcopenia (Taiwan criteria) 8.7% (EWGSOP) 13.5%
Kittiskulnam P, et al. 2017 US	645 haemodialysis patients Age 56.7 ± 14.5 Male 58.6%	Sarcopenia defined by modified EWGSOP criteria Muscle mass definition ① muscle mass / height squared ② muscle mass / body weight ③ muscle mass / body surface area ④ muscle mass / body mass index Handgrip strength Gait speed	Low muscle mass (depends on low muscle by any indexing) Male: 12.2–37.3% Female: 2.3–25.5% Low muscle strength Male: 30.6% Female: 28.8% Slow gait speed Male: 24.7% Female: 48.3% Sarcopenia defined by ① 3.9% ② 11.4% ③ 15.9% ④ 14.0%

Studies Using Psoas Muscle Index (PMI) to diagnose Sarcopenia or PEW

In 2019 study, Homare Okamura, Naoyuki Kimura, Keisuke Tanno et al [76] found that Preoperative sarcopenia defined from the psoas muscle area was associated with long-term outcomes after valve surgery. Thus, the measurement of psoas muscle area can help facilitate more accurate risk scoring in elderly patients.

In 2018, Dae Hoe Gu et al. [77] found Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia in patients with liver cirrhosis and found that PMTH is an independent prognostic factor for mortality in cirrhotic patients.

In 2017, Ranjani N. Moorthi et al. [78] found the clinical relevance of sarcopenia in CKD patients that outcome of sarcopenia in CKD patients was differ than normal populations, which was more severe and outcome can be improved by earlier treatments.

In June 2017, Jukes P.Namm et al. [79] result showed the use of a semi-automated CT sarcopenia metric that estimates psoas muscle size and density, can add important independent predictive value to clinical risk factors for outcomes after PD for pancreatic cancer.

In 2017, Noriko Ishii , Yoshinori Iwata , Hiroki Nishikawa et al. [80] done a study title as Effect of pretreatment psoas muscle mass on survival for patients with unresectable pancreatic cancer undergoing systemic chemotherapy. The study cohort included 31 male and 30 female patients with a median age of 72 years, 13 of whom were stage IVA, and 48 were stage IVB. The median PMI in males was 4.3 cm^2/m^2 (range, 1.6-8.2 cm^2/m^2), while that in females was 2.3 cm^2/m^2 (range, 0.7-6.1 cm^2/m^2). The proportion of patients with performance status 0 in the PMI-High group was significantly high, compared with that in the PMI-Low group [83.3% (25/30) vs. 58.1% (18/31); P=0.0486]. Body mass index in the PMI-High group was significantly higher compared with that in the PMI-Low group (P=0.0154).

In 2016, Glen R. Morrel et al. [81] conducted study titled as Psoas muscle cross-sectional area as a measure of whole body lean muscle mass in maintenance haemodialysis patients and they conclude that psoas muscle area provides a good measure of whole body muscle mass, better than paraspinous muscle area.

In January 2017 Kazuhiro Harada et. al [82] done a study titled as “Impact of Skeletal Muscle Mass on Long-Term Adverse Cardiovascular Outcomes in Patients with Chronic Kidney Disease” as a

result, the rate of the composite of adverse cardiovascular outcomes in the low PMI group was numerically higher than that in the high PMI group. Cox proportional hazards models revealed that the presence of low PMI was independently associated with MACE [hazard ratio (HR), 3.98; 95 % CI, 1.65–9.63; p = 0.0022]

In February 2020 Alice Sabatino et al. [83] published a study titled as "Muscle mass assessment in renal disease: the role of imaging techniques" and stated that CT SCAN is good choice for muscle mass calculation in renal disease because as it is not influenced by hydration status, it can be used in the CKD/ESKD population with better precision than DXA.

In March 2020 P. Lakshmi Prashanthi et al done study as "Standardization of PSOAS Muscle Index Measurements Using Computed Tomography" in Indian populations.

In April 2021 Kiyonori Ito et al. [84] published a study titled as "Muscle mass evaluation using psoas muscle mass index by computed tomography imaging in hemodialysis patients "which result showed HD patients were recruited (31 males and 19 females; HD duration, 9.0 ± 8.8 years). The SMI was 6.10 ± 1.20 kg/m2, and the PMI was 4.79 ± 1.61 cm^2/m^2. Regarding the reliability of PMI measurements, intra-rater reliability [intra-class correlation (ICC) ¼ 0.999] and inter-rater reliability (ICC ¼ 0.998) were high in this study. The mean PMI of male patients was 5.40 ± 1.62 cm^2/m^2, while that of female patients was significantly lower (3.78 ± 0.98 cm^2/m^2; p < 0.001). The PMI was significantly and positively correlated with SMI (r ¼ 0.630, p < 0.001), in addition to HD duration, body mass index (BMI), serum phosphate and serum creatinine (Cr). In the multivariate linear regression analysis by two models using SMI or BMI, they were respectively extracted as an independent factor associating with PMI, in addition to serum Cr and the difference of sex.

In July 2021 Byung Hoon Kwack, Jun Chul Kim et al. [85] done study titled as "Association Between the Normal-Density Psoas Muscle Index and Handgrip Strength or Gait Speed in Maintenance Hemodialysis Patients" as result Correlation coefficients for the SGA score, ASM/Ht^2, HGS, and GS were greater for the NPM index than for the PM index. The linear regression analysis showed that, on multivariate analysis, the NPM index was significantly associated with the SGA score, ASM/Ht^2, and GS.

In September 2021 Takahiro Yajima, Maiko Arao et al. [86] published a study aimed to investigate whether PMTH could accurately predict mortality in patients undergoing hemodialysis. They

examined 207 patients (mean age: 63.1 years; men: 66.2%) undergoing hemodialysis for more than 6 months in hospital affiliated clinic. PMTH was calculated at the L3 vertebra level using CT. Patients were divided according to the PMTH cut-off points: 8.44 mm/m in women and 8.85 mm/m in men; thereafter, they were combined into low and high PMTH groups. PMTH was independently correlated with the simplified creatinine index ($\beta = 0.213$, $P = 0.021$) and geriatric nutritional risk index ($\beta = 0.295$, $P < 0.0001$) in multivariate regression analysis. During a median follow-up of 3.7 (1.8–6.4) years, 76 patients died, including 41 from cardiovascular causes. In the multivariate Cox regression analysis, low PMTH (adjusted hazard ratio, 2.48; 95% confidence interval, 1.36–4.70) was independently associated with an increased risk of all-cause mortality. The addition of binary PMTH groups to the baseline risk model tended to improve net reclassification improvement (0.460, p = 0.060). In conclusion, PMTH may be an indicator of protein energy wasting and a useful tool for predicting mortality in patients undergoing hemodialysis.

In 2021 Kosei Yamaguchi, Mineaki Kitamura et al. [87]done a study titled as “Association between the psoas muscle index and hospitalization for pneumonia in patients undergoing hemodialysis” which was retrospective study, in this study Among 330 patients (mean age, 67.3 ± 13.3; 56.7% male; median dialysis vintage 58 months, (interquartile range [IQR] 23–124), 79 were hospitalized for pneumonia during the observation period (median observation period was 4.5 years [IQR 2.0–9.1]). The multivariable Cox proportional analysis, which was adjusted for age, sex, dialysis vintage, diabetes mellitus, and stroke history and considered death as a competing risk, indicated that decreased PMI/ (standard deviation) was closely associated with the development of pneumonia (hazard ratio: 0.67, 95% confidence interval: 0.47–0.95, $p = 0.03$).

AIMS AND OBJECTIVES

AIM:

- To study association between protein energy wasting **(**PEW**)** and Psoas Muscle Index **(**PMI**)** in patients with CKD.

OBJECTIVES:

Primary objective

- To study Protein Energy Wasting in patients with CKD using biochemical and Anthropometric parameters with correlation of Psoas muscle index as a tool to detect PEW**.**

Secondary objective

- To study prevalence of Protein Energy Wasting (PEW) in patients with CKD.

MATERIALS AND METHODS

The present study was conducted in the Dept. of Nephrology in collaboration with Department of Radiodiagnosis, AIIMS, Jodhpur from January 2020 to October 2021. Ninety (90) patients with Chronic Kidney Disease (stage 3 to 5 ND + Dialysis dependents) were the subjects of the study.

No control group was used. Study was Observational And Cross-sectional.

STUDY SETTING:

Patients attending the out-patient and in-patient services of Department of Nephrology of All India Institute of Medical Sciences, Jodhpur, Rajasthan.

INCLUSION CRITERIA:-

CKD (Stage 3 to 5 ND **+** Dialysis dependent) patients who will be undergoing for CT SCAN KUB region for indications as per existing guidelines.

EXCLUSION CRITERIA: -

1) Chronic illnesses as Tuberculosis, Malignancy, Retro positive, chronic Liver disease (CLD) which leads to malnutrition
2) Patient not willing to give consent for the study
3) Endocrinological disease as thyrotoxicosis, growth hormone deficiency which leads to malnutrition
4) Sepsis
5) Neurological disease which leads to sarcopenia as MND
6) pregnancy
7) Age < 18 yrs.

STUDY DESIGN:

A cross sectional study was conducted after seeking written informed consent from the study participants. Patients were categorized in CKD stages by using The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

Protein Energy Wasting (PEW) diagnosed by the criteria proposed by The International Society of Renal Nutrition and Metabolism (ISRNM).

On the visit to hospital, baseline assessment of various variables were done which includes:

Socio-demographic - Name, age, gender, religion, marital status, educational status and employment status, socioeconomic status.

A detailed medical history was taken. Particular attention was given to duration of disease, Dialysis vintage period, Dietary changes, Weight changes, Gastrointestinal symptoms, Functional capacity and others comorbidities.

A complete physical examination including height in metres and weight in kilogram, waist hip ratio and calculates basal metabolic index (BMI), Hand grip strength, mid upper arm muscle circumference (MAMC) and BP, and pulse rate.

The tests which were carried out in the patients CKD with PEW based on the criteria described above are:

a. Hemoglobin
b. Kidney Function Test (Serum Creatinine & Urea)
c. Serum Total Protein & Albumin
d. Serum Cholesterol
e. Serum Bone & Mineral Panel (Calcium, Phosphorus, Vitamin -D)
f. Intact PTH (iPTH)
g. NCCT KUB to calculate Psoas Muscle Index (PMI)

❖ Anthropometry

Body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters. MAMC was calculated according to the following equation, based on mid-arm circumference (measured at mid-point from the acromion to olecranon) and the triceps skinfold (using caliper)

$$\text{MAMC} = \text{midarm circumference (cm)} - \pi \left[\frac{\text{triceps skinfold (mm)}}{10} \right]$$

Fig no. 11 Shows routine measurement of skinfold thickness

Values of MAMC were compared with the 50th percentile of NHANES II and standard adequacy of <90% was considered as reduced muscle mass [21].

❖ Handgrip strength (HS)

Muscle strength was assessed in the dominant hand using a dynamometer. Patients were first familiarized with the device and then were examined standing with both arms extended sideways from the body with the dynamometer facing away from the body. Patients were instructed to grip the dynamometer with the maximum strength in response to a voice command, and the highest value of three measurements was considered for the study. Handgrip strength (HGS) values under the 30th percentile from a specific-population reference value adjusted for age and sex were considered as reduced.

❖ Subjective global assessment (SGA)

The 7-point SGA was employed to evaluate the nutritional status [89,88]. Briefly, the SGA is based on two major categories: clinical history and physical examination. Clinical history includes five components (weight change, dietary intake change, gastrointestinal symptoms, functional impairment and comorbidities), and physical examination considers aspects such as reduction in muscle and fat, presence of oedema and ascites (both related to nutritional condition). Each of these components is scored from 1 to 7 with the highest value meaning better condition. Then, an overall subjective score is attributed to the patient as 1 to 2 (severely malnourished), 3 to 5 (moderately to mildly malnourished) and 6 to 7 (well nourished). For the purpose of this study, alteration in the physical examination in any of the following sites temples, clavicle, shoulders, spike, pollicis interosseous muscle, knee or quadriceps was considered as muscle wasting.

Serum Creatinine

Creatinine is a metabolic product of creatine and phosphocreatine, which are both found almost exclusively in muscle. Thus, creatinine production is proportional to muscle mass and varies little from day to day.

Measurements of creatinine are used in the diagnosis and treatment of renal disease and prove useful in the evaluation of kidney glomerular function and in monitoring renal dialysis. However, the serum level is not sensitive to early renal damage and responds more slowly than blood urea nitrogen (BUN) to haemodialysis during treatment of renal failure. Both serum creatinine and BUN are used to differentiate prerenal and postrenal (obstructive) azotaemia. An increase in serum BUN without concomitant increase of serum creatinine is key to identifying prerenal azotaemia. In post renal conditions where obstruction to the flow of urine is present e.g. malignancy, nephrolithiasis and prostatism, both the plasma creatinine and urea levels will be increased; in these situations the rise is disproportionately greater for BUN due to the increased back diffusion of urea.

Serum creatinine varies with the subject's age, body weight, race and sex. It is sometimes low in subjects with relatively small muscle mass, cachectic patients, amputees, and in older persons.

Intended Use

Enzymatic assay for the quantitative determination of creatinine in human serum, plasma and urine on Beckman Coulter AU analysers. For *in vitro* diagnostic use only.

Specimen

Serum and heparinised plasma. Stable in serum and plasma for 7 days when stored at 2-25°C.

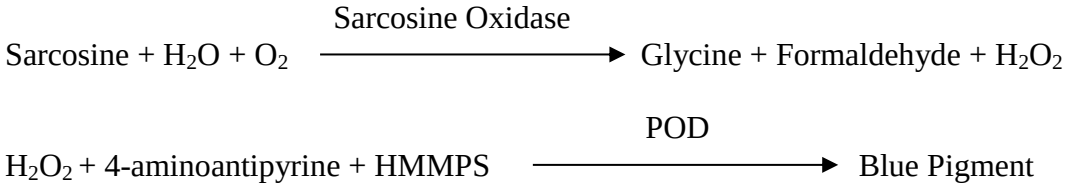
Test Principle

Creatinine is hydrolysed by creatininase to creatine. The creatine formed is hydrolysed by creatinase to sarcosine and urea. Sarcosine oxidase catalyzes the oxidative demethylation of the sarcosine to yield glycine, formaldehyde and hydrogen peroxide. In the presence of peroxidase (POD), the hydrogen peroxide formed reacts by quantitative oxidation condensation with N-(3-sulfopropyl)-3-methoxy-5-methylaniline (HMMPS) and 4-aminoantipyrine to yield a blue pigment. The creatinine concentration is proportional to the change in absorbance at 600/700 nm.

Reaction Principle

$$\text{Creatinine} + H_2O \xrightarrow{\text{Creatininase}} \text{Creatine}$$

$$\text{Creatine} + H_2O \xrightarrow{\text{Creatinase}} \text{Sarcosine} + \text{Urea}$$



Calibration

Use System Calibrator Cat. No. 66300 for the serum and plasma application and Urine Calibrator Cat. No. ODC0025 for the urine application.

The serum calibrator creatinine value is traceable to the Isotope Dilution Mass Spectroscopy (IDMS) method via National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 967.

UREA

Urea is synthesised in the liver as the final product of protein and amino acid metabolism. Urea synthesis is therefore dependant on daily protein intake and endogenous protein metabolism. Most of the urea produced during these metabolic processes is eliminated by glomerular filtration, with 40 – 60% diffusing back into the blood, irrespective of the flow rate in the proximal tubule. Rediffusion in the distal tubule depends on the urinary flow and is regulated by antidiuretic hormone. During diuresis, there is minimal rediffusion of urea into the blood; a large quantity of urea is excreted in the urine and plasma urea concentration is low. During antidiuresis, which may occur in oliguric heart failure, exsiccosis or thirst, urea rediffuses in the tubules at an increased rate and plasma urea is increased. In pre- and post renal kidney failure, the tubular urine flow is decreased, resulting in increased rediffusion of urea in the distal tubules and increased creatinine secretion. Prerenal elevation of urea occurs in cardiac decompensation, increased protein catabolism and water depletion. Urea levels may be elevated due to renal causes such as acute glomerulonephritis, chronic nephritis, polycystic kidney, tubular necrosis and nephrosclerosis. Post renal elevation of urea may be caused by obstruction of the urinary tract.

Intended Use

Kinetic UV test for the quantitative determination of urea in human serum, plasma and urine on Beckman Coulter analysers. For *in vitro* diagnostic use only.

Urea reagent OSR6534 for use on the AU680, AU2700 and AU5400 systems only.

Test Principle [89]

Urea is hydrolysed in the presence of water and urease to produce ammonia and carbon dioxide. The ammonia produced in the first reaction combines with 2-oxoglutarate and NADH in the presence of glutamate-dehydrogenase (GLDH) to yield glutamate and NAD+. The decrease in NADH absorbance per unit time is proportional to the urea concentration.

Reaction Principle

$$\text{Urea} + 2\,H_2O \xrightarrow{\text{Urease}} 2\,NH_4^+ + CO_3^{2-}$$

$$\text{2-Oxoglutarate} + 2\,NH4^+ + 2\,\text{NADH} \xrightarrow{\text{GLDH}} 2\,\text{L-Glutamate} + 2\,NAD^+ + 2\,H2O$$

CALCIUM

Intended Use

Photometric colour test for the quantitative determination of total calcium in human serum, plasma and urine on Beckman Coulter AU analysers. For *in vitro* diagnostic use only.

Summary

Measurement of calcium is used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease, urolithiasis and tetany (intermittent muscular contractions or spasms).

Total serum calcium is composed of three fractions: free or ionised calcium, 50%; protein bound calcium most of which is bound to albumin with only a small portion bound to globulins, 45%; and complex-bound calcium, mainly to phosphate, citrate, and bicarbonate, 5%. The ionised calcium is physiologically most significant, but has proven difficult to assay directly. It may be estimated from total calcium given knowledge of the protein content and pH of the blood, which strongly affect the level of ionised calcium.

Test Principle [90]

Calcium ions react with o-Cresolphthalein-complexone in an alkaline medium to form a purple coloured complex. In this method the absorbance of the Ca-oCPC complex is measured

bichromatically at 570/660 nm. The resulting increase in absorbance of the reaction mixture is directly proportional to the calcium concentration in the sample.

Reaction Principle

$$Ca^{2+} + \text{o-CPC} \xrightarrow[\text{pH 10.6}]{\text{8-Hydroxyquinoline}} \text{Ca-o CPC Complex}^{2+} \text{ (purple)}$$

PHOSPHOROUS

Intended Use

Photometric UV test for the quantitative determination of inorganic phosphorous in human serum, plasma and urine on Beckman Coulter analysers. For *in vitro* diagnostic use only.

Summary

In plasma and serum the majority of phosphate exists in the inorganic form (Pi), approximately 15% bound to protein and the remainder in complexed and free forms. Serum phosphate concentrations are dependent on diet and variation in the secretion of hormones such as PTH.

Daily Phosphorus Balance At steady state, oral phosphorus intake is balanced by phosphate (Pi) excretion in the urine and feces (Figure 1B). Daily phosphorus intake varies between 700 and 2000 mg, depending on consumption of phosphorus-rich foods, such as dairy products. After absorption, phosphorus is transported across cell membranes as phosphate (31 mg/l elemental phosphorus51 mmol/l phosphate). Phosphate in the plasma or extracellular fluid undergoes one of three fates: transport into cells, deposition in bone or soft tissue, or elimination predominantly by the kidneys. Within the body, the majority of phosphorus stores are in the bone. Although serum phosphate (Pi) levels constitute ,1% of total body phosphorus stores, maintenance of serum Pi within a relatively narrow range (2.5–4.5 mg/dl in adulthood) is crucial for several important cellular processes, including energy metabolism, bone formation, signal transduction, or as a constituent of phospholipids and nucleic acids (20). Maintenance of serum phosphate within the normal range depends on a complex interplay between absorption of phosphate in the gut, exchange with bone stores, shifts between intracellular and intravascular compartments, and renal excretion.

Test Principle [91]

Inorganic phosphorous reacts with molybdate to form a heteropolyacid complex. The use of a surfactant eliminates the need to prepare a protein free filtrate. The absorbance at 340/380 nm is directly proportional to the inorganic phosphorous concentration in the sample.

Reaction principle

$7\ H_3PO_4 + 12\ (Mo_7O_{24})^{6-} + 72\ H^+ \longrightarrow 7\ H_3PO_4\ (MoO_3)12 + 36\ H_2O$

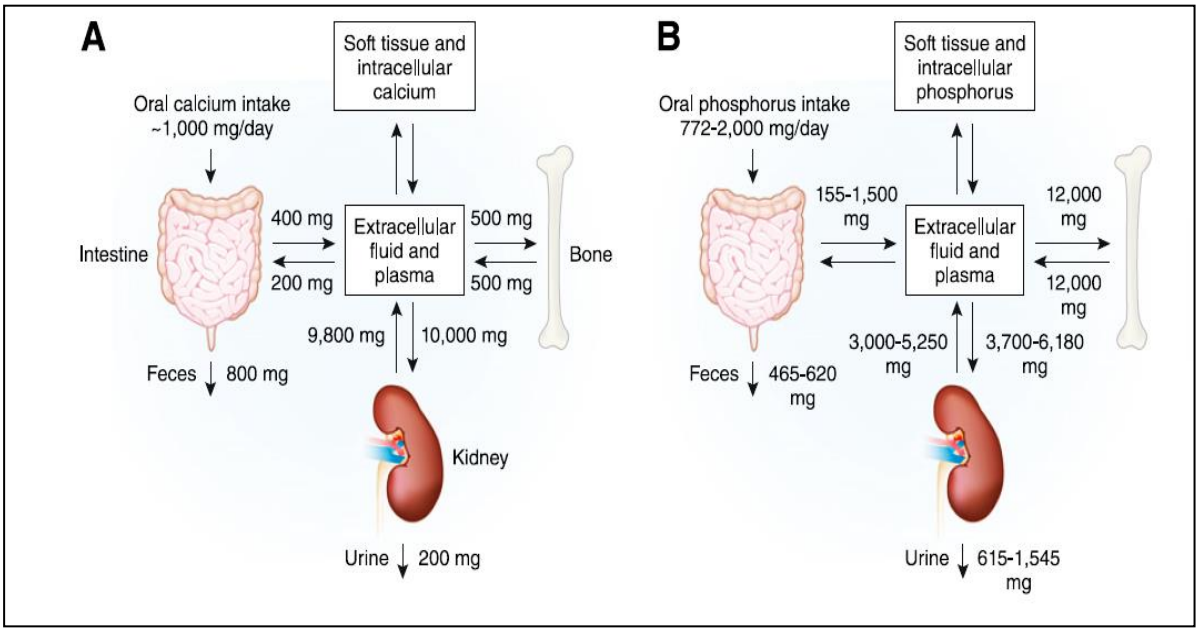


Fig no. 12 Calcium and Phosphate flux between body compartments.
Calcium (A), phosphate (B)

Total Protein

Intended Use

Photometric colour test for the quantitative determination of total protein in human serum and plasma on Beckman Coulter AU analysers. For *in vitro* diagnostic use only.

Specimen

Serum, EDTA or heparinised plasma.

Stable in serum and plasma for 4 weeks when stored at 2-8°C and 6 days when stored at 15-25°C.

Test Principle [92]

Cupric ions in an alkaline solution react with proteins and polypeptides containing at least two peptide bonds to produce a violet coloured complex. The absorbance of the complex at 540/660 nm is directly proportional to the concentration of protein in the sample.

Reaction Principle

$$\text{Protein} + Cu^{2+} \xrightarrow{OH^-} \text{Blue violet complex}$$

Calibration

System Calibrator Cat. No. 66300.

The calibrator total protein value is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 927C

ALBUMIN

Intended Use

Photometric colour test for the quantitative determination of albumin in human serum and plasma on Beckman Coulter analysers.

Specimen

Serum, EDTA or heparinised plasma.

Stable in serum and plasma for 4 weeks when stored at 2-8°C and 6 days when stored at 15-25°C.

Test Principle [93]

A coloured complex is formed when bromocresol green reacts with albumin. The absorbance of the albumin-BCG complex is measured bichromatically (600/800nm) and is proportional to the albumin concentration in the sample.

Reaction Principle

$$\text{Albumin} + \text{Bromocresol} \xrightarrow{\text{pH 4.2}} \text{Green Green Complex}$$

Calibration

System Calibrator Cat. No. 66300.

The calibrator albumin value is traceable to IFCC (International Federation of Clinical Chemistry) standard CRM 470.

Intact human parathyroid hormone (iPTH)

Parathyroid Hormone Physiologic Role

- PTH is secreted by the parathyroid glands in response to hypocalcemia, hyperphosphatemia, and/or calcitriol deficiency
- Minute-to-minute concentrations of PTH are most sensitive to low ionized calcium concentrations
- The sensitivity of this response may be blunted in the presence of hyperphosphatemia in CKD

Intact PTH

- This 84–amino acid protein is cleaved from pre-pro PTH in the parathyroid gland [94].
- Intact PTH (iPTH) has a short half-life (2-4 minutes)
- Cleaved into amino-terminal, carboxy-terminal, and midlength fragments, which are metabolized in the liver and kidney

- Amino-terminal fragments remain active; carboxy-terminal fragments accumulate in CKD

PTH Assays

- First-generation assays
  - Radioimmunoassay using an antibody against the mid region or carboxy-terminal end
  - Detects full-length PTH and the multiple carboxy- and amino-terminal fragments
  - Unreliable
- Second-generation assay/iPTH assays/2-step first generation immunoradiometric assays (IRMAs)
  - Involve 2 antibodies, one that detects the amino terminus and the other detects the carboxy terminus
  - Most commonly used assay in clinical practice
  - However, in addition to detecting full-length PTH, it also detects fragments commonly referred to as 7-84 PTH
  - This 7-84 PTH may have effects antagonistic to full-length PTH on bone
- Third-generation assays/whole PTH assays/ biointact PTH assays detect only 1-84 PTH

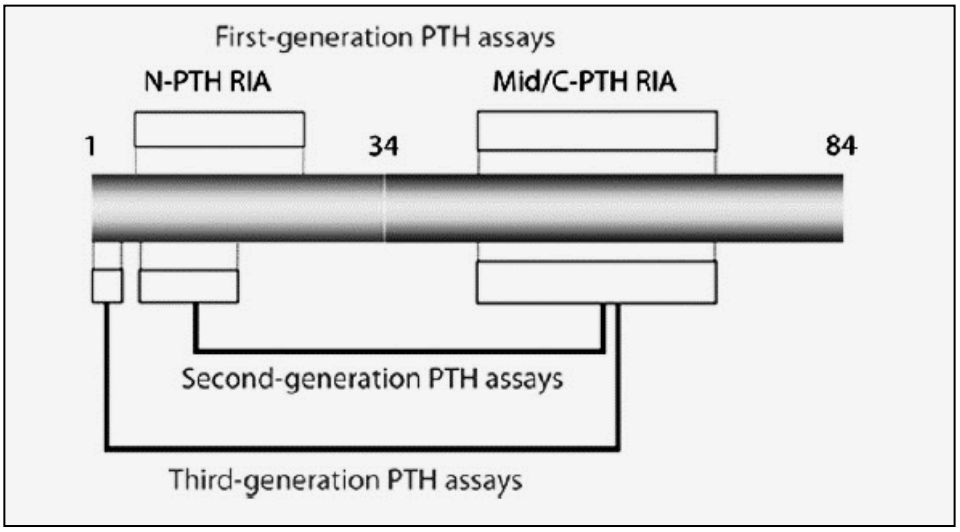


Fig. 13- Assays for parathyroid hormone (PTH). The intact PTH molecule is composed of 84 amino acids; different regions of the protein are targeted by first- through third-generation assays.

INTENDED USE

The LIAISON® N-TACT® PTH Gen II is an *in vitro* chemiluminescent immunoassay (CLIA) intended for the quantitative determination of intact human parathyroid hormone in serum, EDTA and Lithium Heparin plasma samples. Measurements of parathyroid hormone levels are used in the differential diagnosis of hypercalcemia and hypocalcemia resulting from disorders of calcium metabolism.

The test is to be performed on the LIAISON® Analyzer family

SPECIMEN COLLECTION AND PREPARATION

Human Serum, SST serum, EDTA plasma and Lithium Heparin plasma may be used in this assay. Blood should be collected aseptically by venepuncture. Serum samples should be allowed to clot, and the serum separated from the clot as soon as possible. Plasma samples should be centrifuged and removed from the cells immediately after centrifugation. Samples having particulate matter, turbidity, lipemia, or erythrocyte debris may require clarification by filtration or centrifugation before testing. Grossly haemolyzed or lipemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination should not be tested.

PRINCIPLE OF THE PROCEDURE

The LIAISON® N-TACT® PTH Gen II assay is a modified 2-step, 2-site sandwich assay that uses 2 polyclonal antibodies for capture and detection of intact PTH. The assay uses 150 µL of calibrator, control or patient sample incubated with an assay buffer and an isoluminol conjugated polyclonal affinity purified antibody to the 1-34 region of the 1-84 PTH molecule. Following incubation, paramagnetic particles coated with a second polyclonal antibody with a tendency to bind in the C terminal region (39-84) of the 1-84 PTH molecule are added to the reaction and incubated. After the second incubation, the unbound material is removed with a wash cycle. The starter reagents are then added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as relative light units (RLU) and is proportional to the concentration of intact PTH present in the calibrators, controls or samples.

VITAMIN-D

Vitamin D is a steroid hormone involved in the intestinal absorption of calcium and the regulation of calcium homeostasis. Vitamin D is essential for the formation and maintenance of strong, healthy bones.

Vitamin D deficiency can result from inadequate exposure to the sun, inadequate alimentary intake, decreased absorption, abnormal metabolism, or vitamin D resistance.1 Recently, many chronic diseases such as cancer,2–4 high blood pressure,5 osteoporosis,6,7 and several autoimmune diseases8–10 have been linked to vitamin D deficiency.

Whether consumed or produced, both forms of vitamin D (D2 and D3) are metabolized by the liver to 25(OH)vitamin D, and then converted in the liver or kidney into 1,25-dihydroxyvitamin D.11 Vitamin D metabolites are bound to a carrier protein in the plasma and distributed throughout the body. The most reliable clinical indicator of vitamin D status is 25(OH)vitamin D because serum and plasma 25(OH)vitamin D levels reflect the body's storage levels of vitamin D, and 25(OH) vitamin D correlates with the clinical symptoms of vitamin D deficiency.12

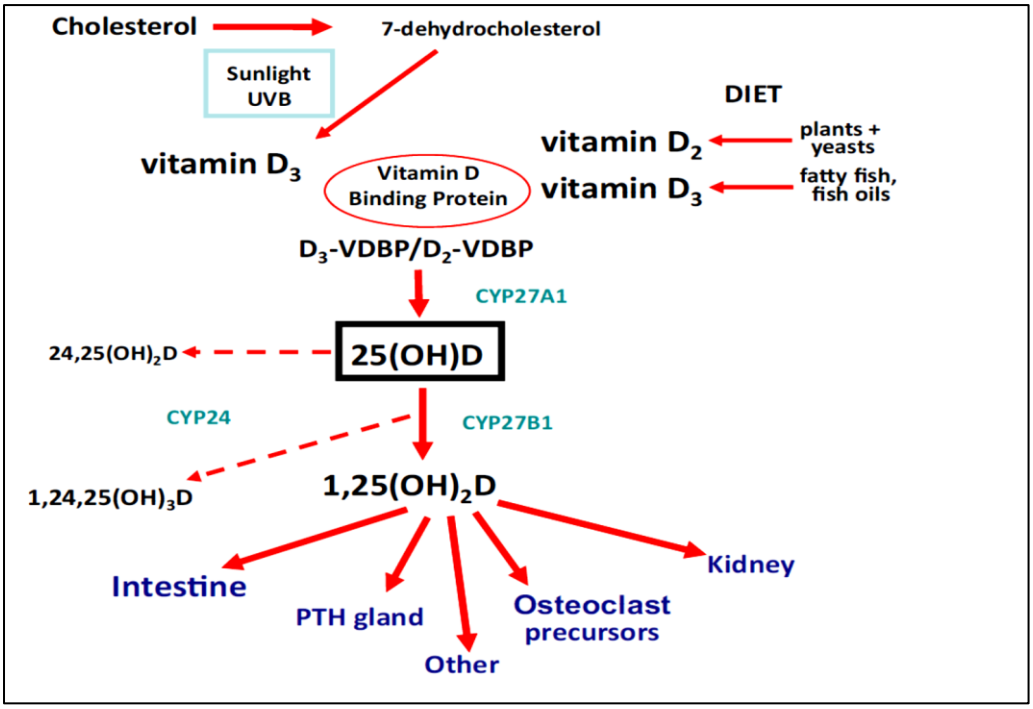


Fig. 14 Overview of vitamin D metabolism.

Specimen Collection and Handling

Human serum and plasma (EDTA, lithium-heparin, sodium-heparin) are the recommended sample types for this assay.

Principles of the Procedure

The ADVIA Centaur VitD assay is an 18-minute antibody competitive immunoassay that uses an anti-fluorescein monoclonal mouse antibody covalently bound to paramagnetic particles (PMP), an anti-25(OH)vitamin D monoclonal mouse antibody labeled with acridinium ester (AE), and a vitamin D analog labeled with fluorescein.

An inverse relationship exists between the amount of vitamin D present in the patient sample and the amount of relative light units (RLU) detected by the system.

PSOAS MUSCLE INDEX (PMI cm^2/m^2)

The diagnosis PEW was based on defined criteria proposed by ISNRM including Biochemical parameter the presence of derangements in both muscle function and muscle mass and dietary intake.

In our study After positioning the patient on the CT table and appropriate immobilization measures were taken to prevent patient fall and also to avoid motion artefacts. CT with the above mentioned protocols were carried out with anatomical coverage extending from diaphragm to symphysis pubis. The scan was obtained during a single breath hold for 5-9 secs approximately. Image reconstruction from the acquired image data were performed with an parameters: effective slice thickness of 0.75mm (retrospective reconstruction).The data sets were transferred to a Philips advanced workstation and post-processing of the images namely multiplanar reconstruction (MPR) were performed.

Measurement protocol

CT images were acquired by SOMATOM Definition Flash dual energy source 2x128 slice CT scanner (Siemens Healthcare GmbH, Germany).

To calculate Psoas Muscle Index (PMI) we used Manual Tracing (MT) method using RadiAnt DICOM viewer version 2021.2(64-bit) software.

Technique

Step 1: Select the axial image at the level of L3 vertebrae for Area analysis and obtained coronal section corresponded to axial image at the level of lower border of L3 vertebrae as mentioned below image.

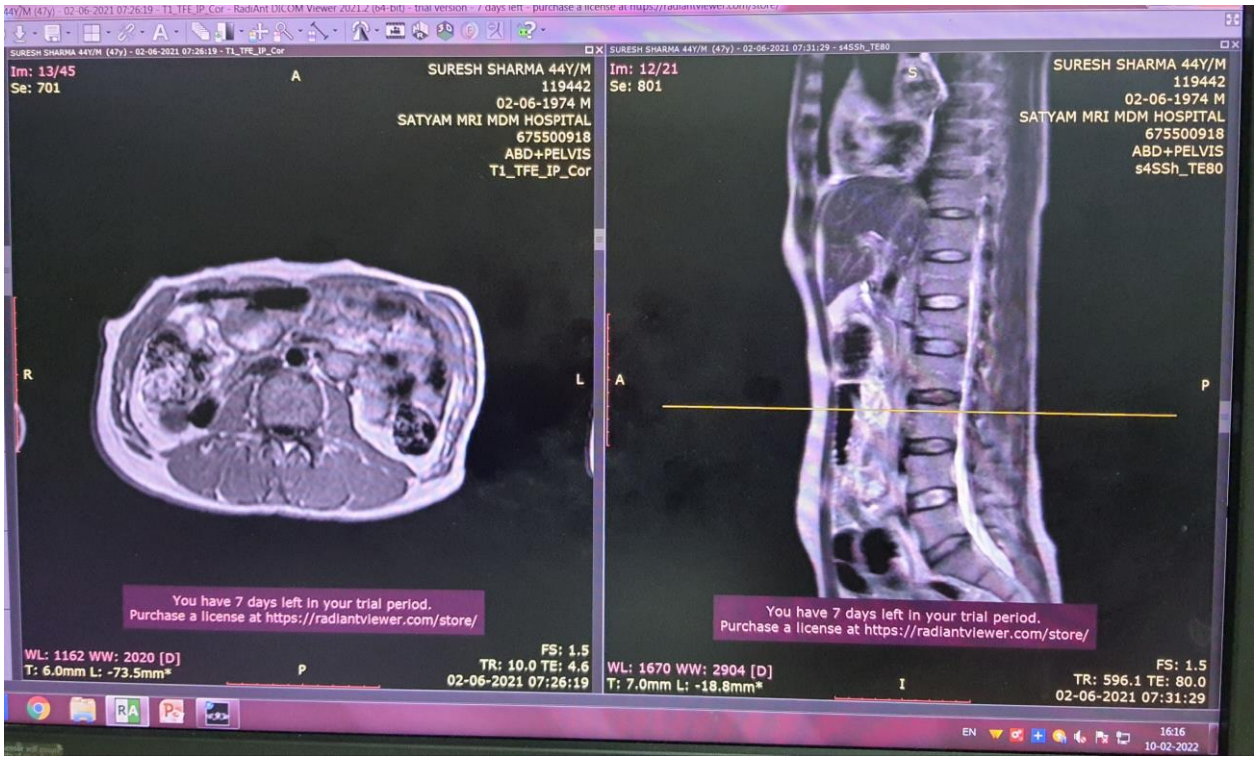


Fig no.15 Represent axial and coronal view image of Psoas Muscle at the level of L3 vertebrae

Step 2: Click the segment menu and select the measurements icon. After selecting closed polygon in measurement tools followed by calculation of psoas muscle area by manual tracing (MT) method. Select the apply icon and select the free form ROI icon. Segmentation of the psoas muscle was performed by using a line tracing of a free form ROI on the selected slice and then select apply icon.

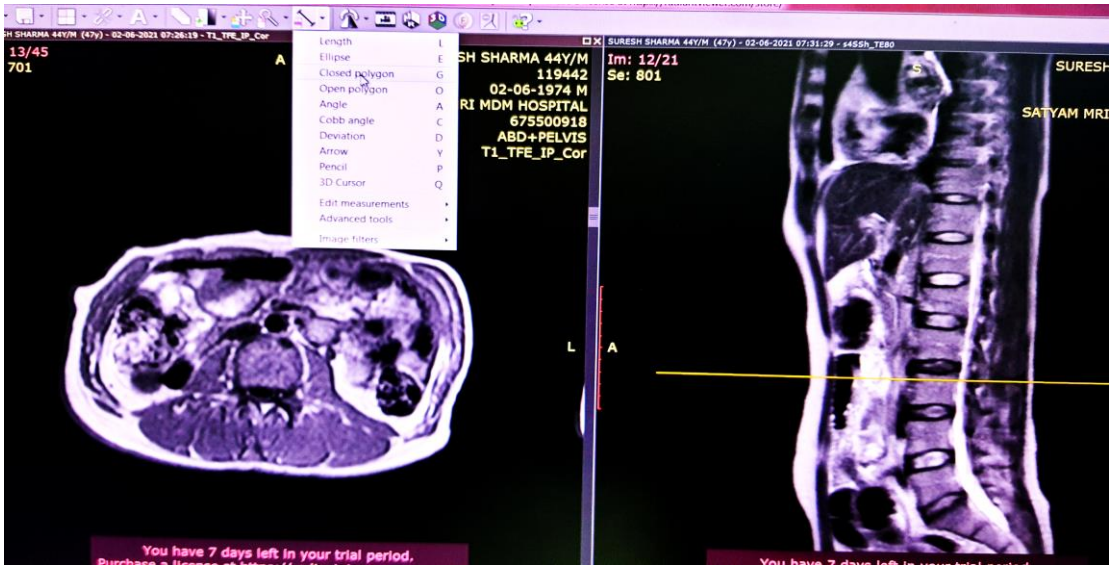


Fig no. 16 Represent measuring method for PMI

Step 3: Click on to display menu and select the area icon**.** Click the right psoas muscle on the window and the outline is drawn to measure the area**.** Subsequently measure the left Psoas muscle and calculate the total psoas area The total psoas area was then normalized for height as per convention for body composite measurements (TPA in square millimeter / square meter).

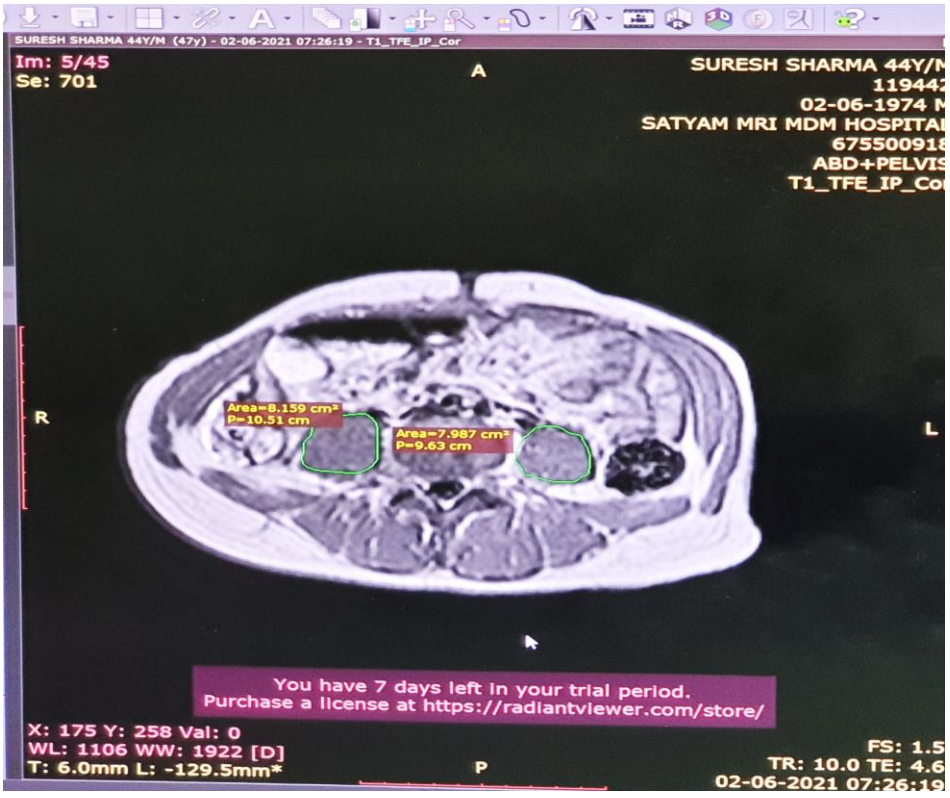


Fig no. 17 Shows Manual Tracing (MT) method to calculate Psoas muscle area (PSA)

The cross-sectional area of the bilateral psoas muscle was measured at the lower border of the third lumbar vertebra (L3) using the manual trace (MT) method. In brief, psoas muscle mass was calculated by tracing the psoas muscles along the psoas marginal line visually using the (RadiAnt DIACOM viewer) radiological software. The evaluation was performed with Radiologist who was trained to use this approach. If the psoas muscle marginal line was unclear due to compression fractures of the vertebrae, the final measurement was decided after discussion by the two physicians. Subsequently, the PMI was calculated as the cross-sectional area of the bilateral psoas muscle (lower border of L3)/height^2(cm^2/m^2).

DATA COLLECTION:

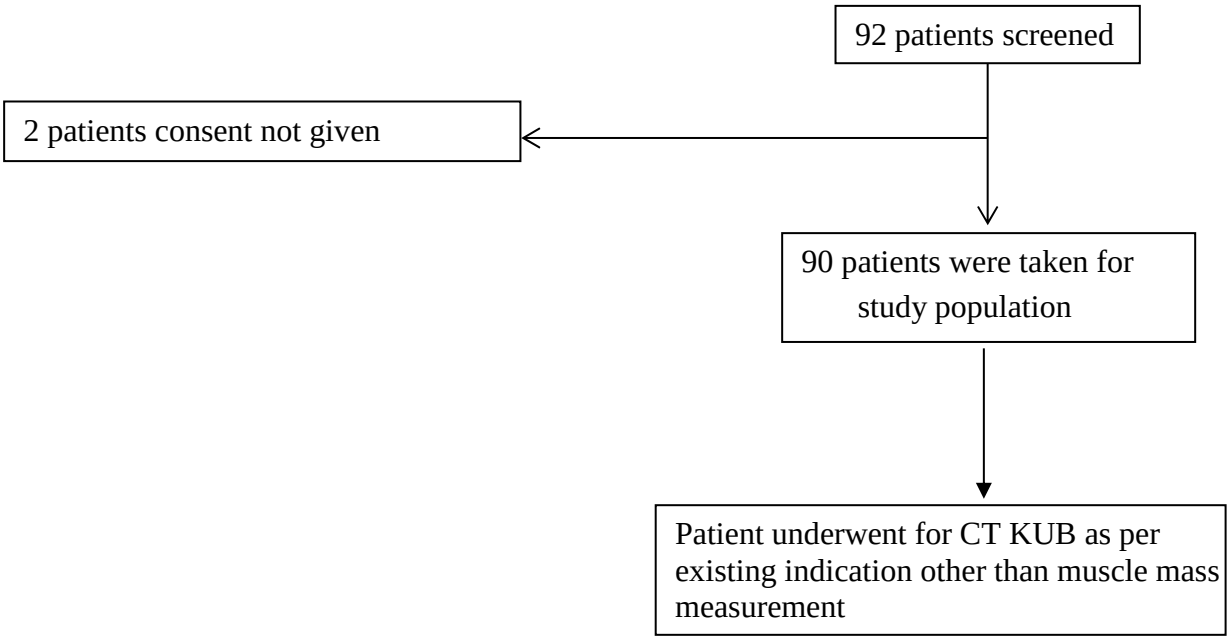
Data were collected on the first visit after obtaining informed written consent for the baseline assessment using following socio-demographic and clinical pro-forma.

Blood and urine samples were taken on the same day and was collected in Vacutainer™ serum separator tubes containing spray-coated silica and clot activator and serum separator gel for serum separation.

STATISTICAL ANALYSIS:

Statistical analysis was carried out using software program SPSS version 25.0. (SPSS Inc. Chicago, USA). Data were presented as mean ± standard deviation for parametric data, or number (%) and median with IQR for non-parametric data unless specified.
The paired Student's t-test was used to compare two parameters.
Correlations between PMI and clinical factors were evaluated by Pearson's correlation coefficient and simple linear regression analysis. Normally distributed data was analysed using unpaired t-test. For determining association between various factors, multivariate linear regression analysis was used. A p value < 0.05 was considered as statistically significant.

CONSORT DIAGRAM



.

OBSERVATION AND RESULTS

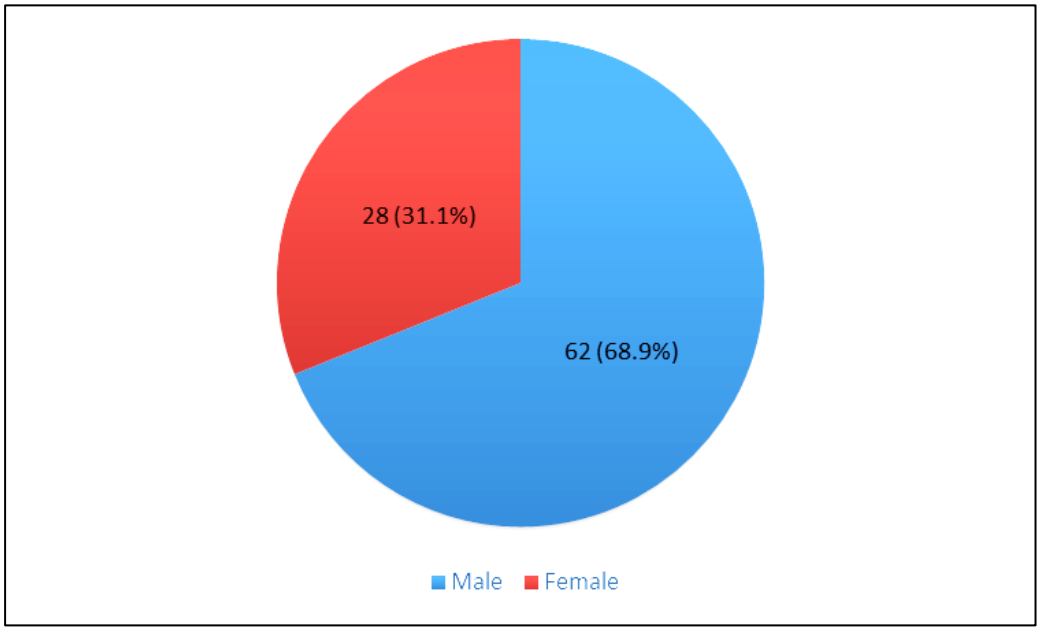
The present study was conducted in the Department of Nephrology and Radiodiagnosis, AIIMS,Jodhpur from February 2020 to October 2021.Patients with CKD (stage 3 to 5+Dialysis dependents) were the study subjects. The total number of enrolled patients were Ninety (90). No controls were enrolled.

AGE (in years)	Mean± SD	Sex		Total (%)
		Male (%)	Female (%)	
10-20	18±1.41	02	00	02
21-30	25.63±3.074	08	03	11
31-40	36.50±3.696	03	01	04
41-50	45.56±2.79	16	07	23
51-60	56.04±3.15	17	07	24
61-70	64.38±2.88	12	08	20
71-80	76.00 ±2.44	04	02	06
Total	51.81±14.61	62	28	90

Table 08 Shows the age and sex distribution of the study population. The mean age of the study population was 51.81± 14.61 years with maximum numbers of patients (26.66%) in the age group of 51-60 years. There were more males (68.9%) than females (31.1%) and the M:F ratio was 2.21.

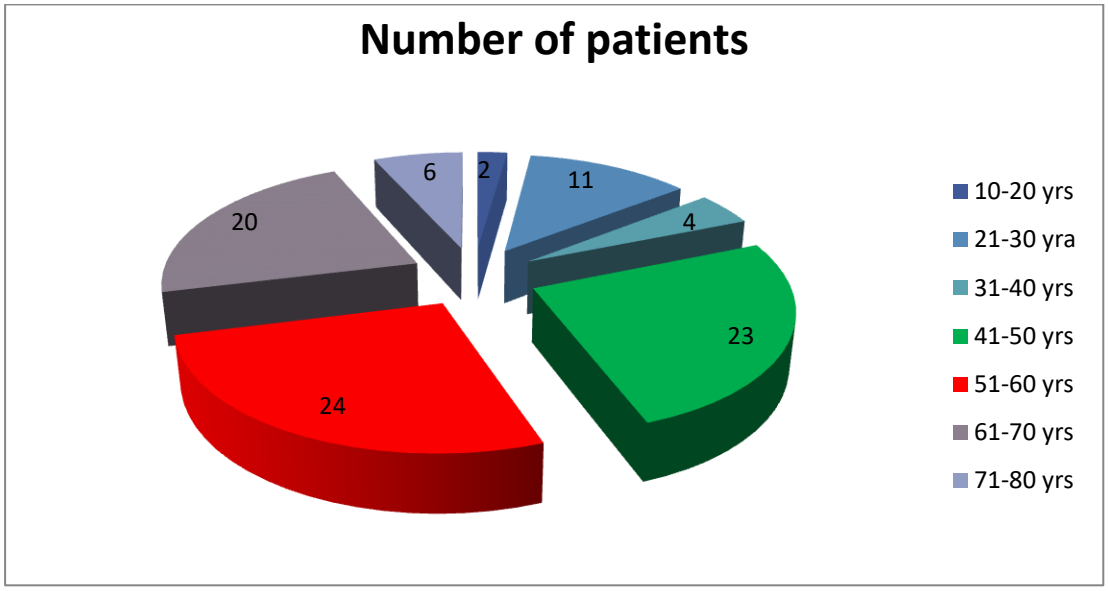
Sex	Number of patients
Male	62 (68.9%)
Female	28 (31.1%)
Total	90 (100%)

Table no 09 Shows Gender Distribution in study population.



Age distribution group	Number of patients
10-20 yrs	02 (2.22%)
21-30 yrs	11 (12.2%)
31-40 yrs	04 (4.45)
41-50 yrs	23 (25.5%)
51-60 yrs	24 (26.6%)
61-70 yrs	20 (22.2%)
71-80 yrs	06 (6.6%)
Total	90

Table No.10 Shows Number of patients in specified age distribution group in study populations with maximum numbers of patients (26.6%) in the age group of 51-60 years and minimum (2.22%) in the age group of 10-20 yrs.



Sex	Number of Patients	Mean ± SD (age)
Male	62	50.5 ± 13.9
Female	28	54.71 ± 15.93
Total	90	51.81±14.61

Table no. 11 shows age and sex distribution in study population

Syndromic Diagnosis	Number of Patients	Mean ± SD (age)
CTIN	73 (81.12%)	53.92 ± 14.11
CGN	17 (18.88%)	41.26 ± 12.75
Total	90	51.81 ± 14.61

Table no.12 Shows age and sex distribution in syndromic diagnosis group in CKD with maximum patients (83.33%) in CTIN group.

CTIN (Total patients = 73) ➢ Obstructive Uropathy = 61 • Renal Stone Disease=52 • Urethral Stricture = 03 • BPH= 06 ➢ CKDu = 11 ➢ Granulomatous inflammation = 01
CGN (Total patients = 17) ➢ Membranous Nephropathy = 02 ➢ Amyloidosis=01 ➢ FSGS=02 ➢ Hypertensive nephrosclerosis =12

Table no. 13 Etiology of CKD

Syndromic Diagnosis (CKD groups)	**Number of patients**
CTIN	73 (81.12%)
CGN	17 (18.88%)
Total	90 (100%)

Table No.14 Shows Number of patients in term of Syndromic Diagnosis of CKD in study populations with maximum number of patients (81.12%) were in CTIN group followed by in CGN group (18.88%).

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
GFR	90	3	58	19.60	14.081
BMI	90	13.14	25.91	19.8456	3.19787
Handgrip	90	5	40	20.98	7.891
MUAC	90	8.0	34.0	21.764	3.7599
PMI	90	1.555	7.999	4.112	1.835
HB	90	4.9	16.0	8.692	2.1134
Creatinine	90	1.770	12.070	4.98148	2.358702
urea	90	44	369	112.77	50.401
Cholesterol	90	42	229	114.12	46.334
Triglyceride	90	62	278	142.92	54.186
Total Protein	90	3.59	8.94	6.3741	1.04036
Albumin	90	1.10	5.00	3.0791	.76709
PTH	90	13.4	1900.0	303.258	290.7621
Vit.-D	90	4.52	45.50	18.0440	8.09435
CALCIUM	90	4.16	13.14	8.4509	1.23121
PHO	90	2.80	10.62	5.3266	1.70664

Table no.15 Shows Baseline characteristic in term of physical and clinical parameters in the study population.

Correlations

		PTH	CALCIUM	Vit.-D	PHOS.
PTH	Pearson Correlation	1	-.158	-.128	.262*
	Sig. (2-tailed)		.137	.230	.013
	N	90	90	90	90
CALCIUM	Pearson Correlation	-.158	1	.172	-.119
	Sig. (2-tailed)	.137		.106	.263
	N	90	90	90	90
Vit.- D	Pearson Correlation	-.128	.172	1	-.119
	Sig. (2-tailed)	.230	.106		.266
	N	90	90	90	90
PHOS.	Pearson Correlation	.262*	-.119	-.119	1
	Sig. (2-tailed)	.013	.263	.266	
	N	90	90	90	90

*. Correlation is significant at the 0.05 level (2-tailed).

Table no. 16 Represent correlation using Pearson test among biochemical parameters in study populations.PTH correlated with Phosphorus but not correlate with calcium and vitamin D

Correlations

		PMI	BMI	Handgrip	MUAC	CHOL	PTH	ALB.
PMI	Pearson Correlation	1	.522**	.529**	.403**	.276**	.003	.253*
	Sig. (2-tailed)		.000	.000	.000	.008	.974	.016
	N	90	90	90	90	90	90	90

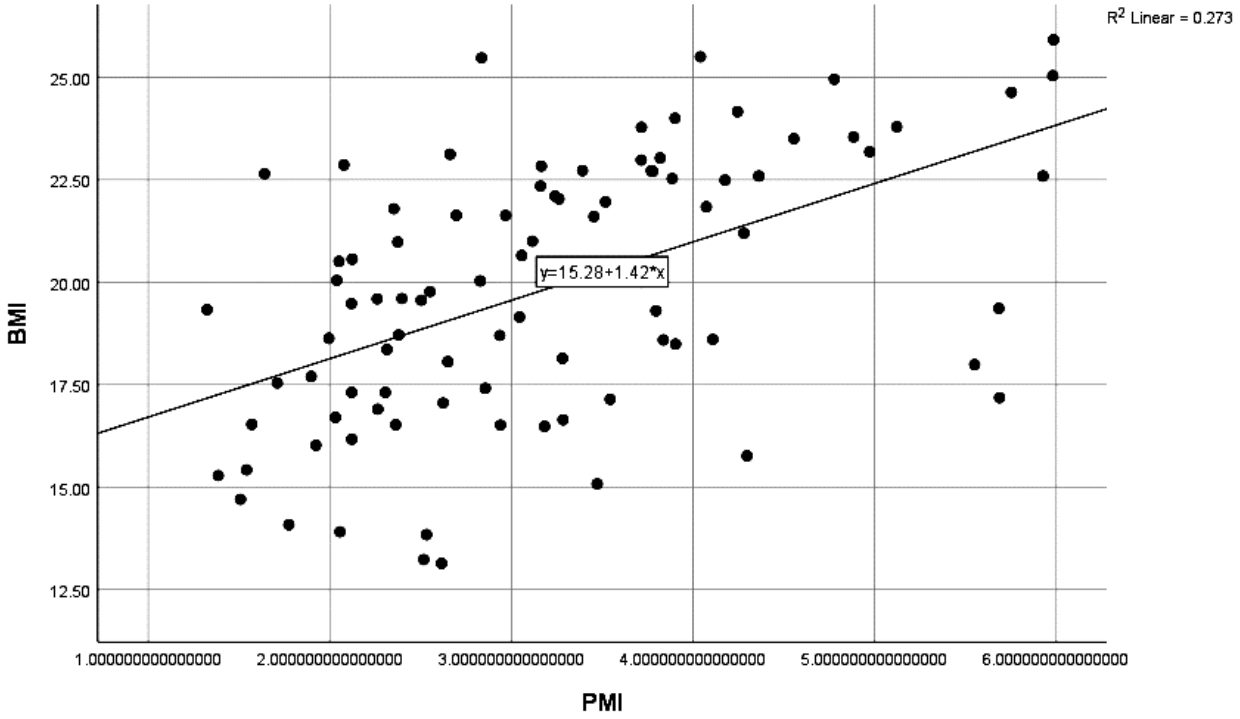
**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

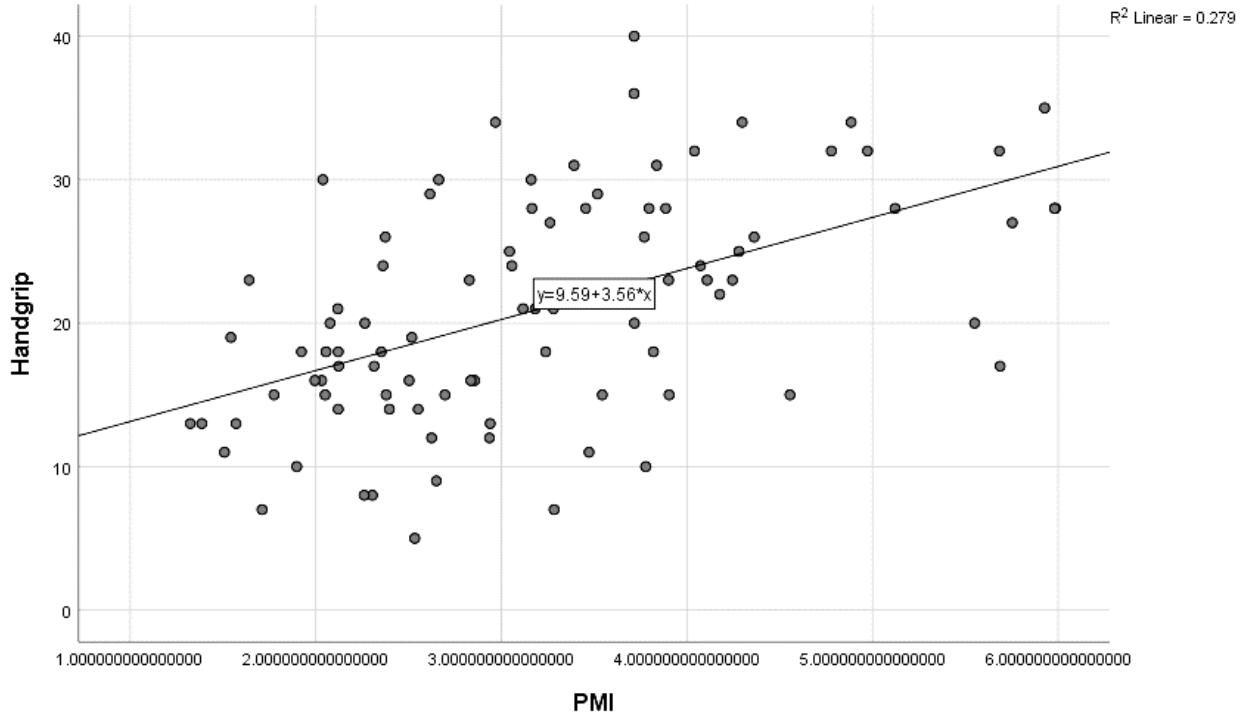
Table no. 17 Represents correlation of PMI with Biochemical and physical parameters in study populations. PMI was correlated with BMI, Handgrip and MUAC which was statistically significant(P value < 0.01) in Physical parameters.
PMI also correlated with cholesterol and Albumin in biochemical parameters (P value < 0.05)

			PMI	SGA-7 POINT	Age groups	GENDER (Male=1, Female=2)	CKD Stage (CKD3=1, CKD4=2 CKD5=3)
Spearman's rho	PMI	Correlation Coefficient	1.000	.434**	-.580**	-.504**	-.124
		Sig. (2-tailed)	.	.000	.000	.000	.243
		N	90	90	90	90	90
	SGA-7 POINT	Correlation Coefficient	.434**	1.000	-.113	-.205	-.262*
		Sig. (2-tailed)	.000	.	.290	.052	.013
		N	90	90	90	90	90
	Age group	Correlation Coefficient	-.580**	-.113	1.000	.105	-.199
		Sig. (2-tailed)	.000	.290	.	.324	.060
		N	90	90	90	90	90
	GENDER (Male=1,Female=2)	Correlation Coefficient	-.504**	-.205	.105	1.000	.149
		Sig. (2-tailed)	.000	.052	.324	.	.161
		N	90	90	90	90	90
	CKD stage category (CKD3=1, CKD4=2 CKD5=3	Correlation Coefficient	-.124	-.262*	-.199	.149	1.000
		Sig. (2-tailed)	.243	.013	.060	.161	.
		N	90	90	90	90	90

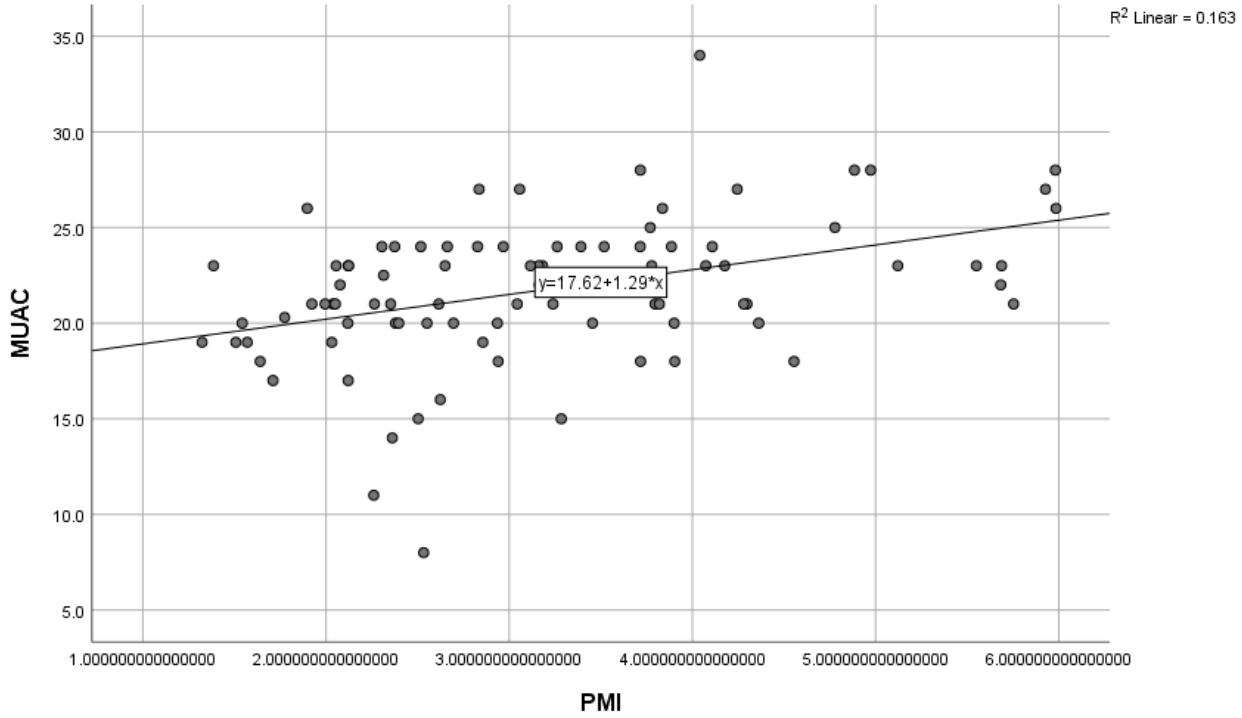
Table no.18 Represents correlation of PMI with SGA, Age, Gender and CKD stages. PMI was positive correlate to SGA and negatively correlate to Age and CKD stage. PMI also correlated with gender.PMI was more in Male group as compared Female group



Graph no. 01 : Scatter plot diagram showing correlation between Psoas muscle index(PMI) and Body mass index (BMI) which was statistically significant.



Graph 2 : scatter plot diagram showing correlation between Psoas muscle index(PMI) and Handgrip (BMI) which shows strong correlation.



Graph 3 : scatter plot diagram showing correlation between Psoas muscle index(PMI) and Mid upper arm circumference (MUAC) which was statistically significant.

SGA Score (7 - points score)	Number of patients
6-7 (well nourished)	13
3-5 (moderate to severely malnourished)	65
1-2 (severaly malnourished)	12
Total	90

Table no. 19 shows number of patients with SGA score in study population with maximum patients(72.22%) were moderate to severely malnourished (SGA score 3-5)

CKD Stages	Number of patients
CKD-3	19
CKD-4	21
CKD-5	50
Total	90

Table No.20 shows number of patients in different CKD stage with maximum patients (55.5%) in CKD stage 5.

RRT (HD + PD)	Number of patients
Required	64 (71.1%)
Not required	26(28.9%)
Total	90

Table no.21 shows RRT requirement in study population with patients (71.1%) were received RRT

.

Sex	Number of Patients	PMI Mean ± SD
Male	62	4.512 ± 1.929
Female	28	3.228 ± 1.231
Total	90	4.112 ± 1.835

Table no. 22 shows mean Psoas muscle index (PMI) in study populations. The mean PMI in study population was 4.112 ± 1.835. It was significantly higher in Male group (4.512 ± 1.929) than Female group (3.228 ± 1.231) with P value being <0.001

P value and statistical significance: The two-tailed P value equals 0.0017

The mean of Female minus Male equals -1.283500

Groups of CKD (Syndromic Diagnosis)	Number of Patients	PMI Mean ± SD
CTIN	73	3.498 ± 1.200
CGN	17	7.50 ± 0.422
Total	90	4.112 ± 1.835

Table no. 23 shows mean Psoas muscle index (PMI) in study populations. The mean PMI in study population was 4.112 ± 1.835. It was significantly higher in CGN group (7.50 ± 0.422) than CTIN group (3.498 ± 1.20) with P value being <0.001

The two-tailed P value is less than 0.0001

The mean of CTIN minus CGN equals -4.002000

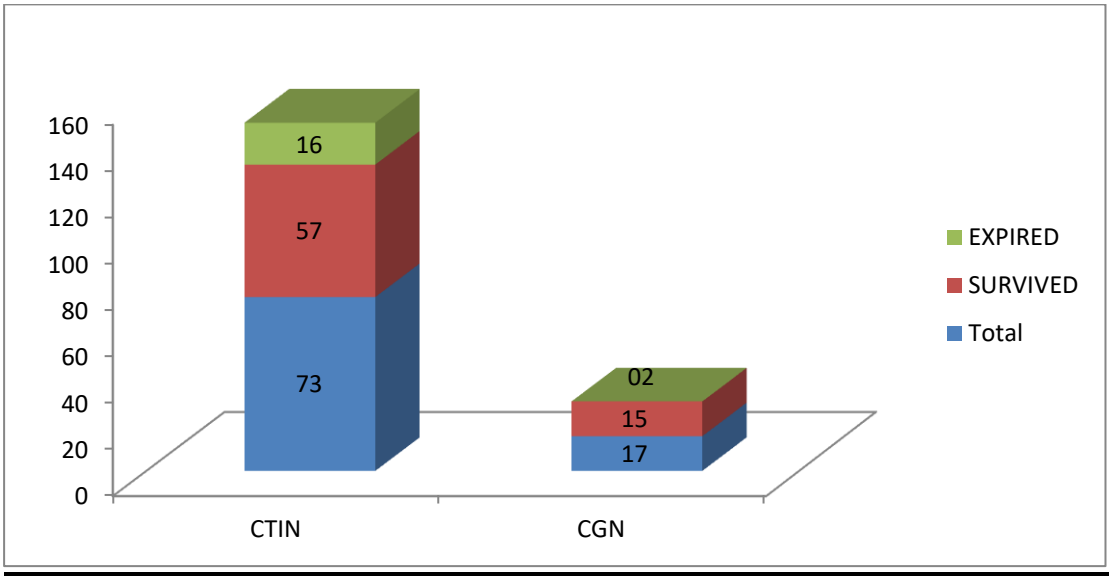
Groups CKD (Syndromic Diagnosis)	Number of patients Survived	Number of patients Expired	Total
CTIN	57	16	73
CGN	15	02	17
Total	72	18	90

Table 24 shows outcome in patients in CKD groups (Syndromic Diagnosis).

The mortality was 20% in study population with 17.8% in CTIN group.

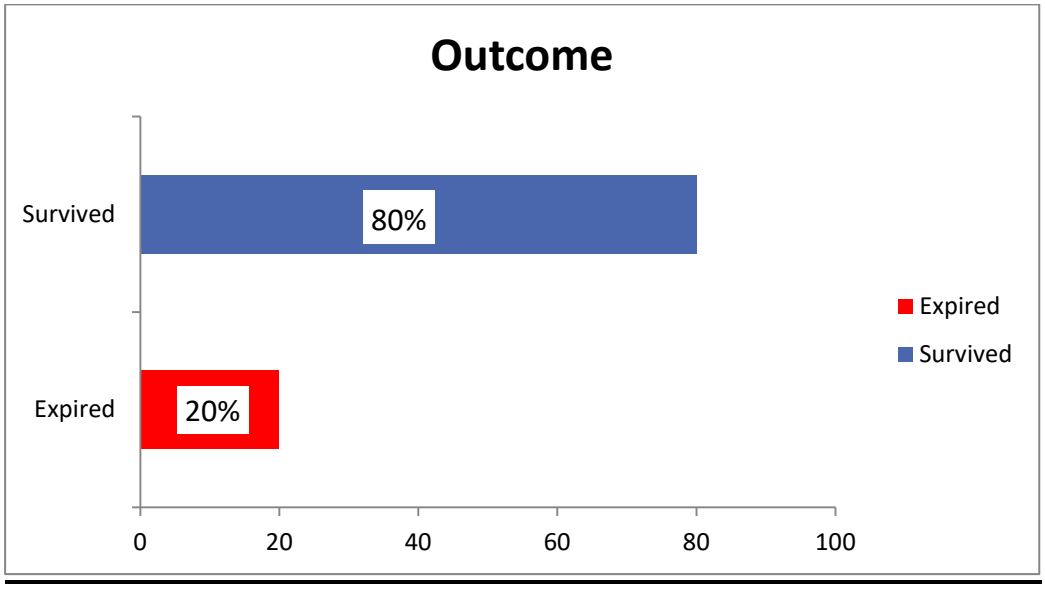
There was a statistically significant difference in mortality among CKD groups

P-value <0,001.



OUTCOME	Number of Patients	Percentage
SURVIVED	72	80
EXPIRED	18	20
Total	90	100.0

Table no.25 Shows outcome in study population. In our study 20 % patients were expired.



OUTCOME	Number of Patients	PMI Mean ± SD
SURVIVED	72	4.53 ± 1.749
EXPIRED	18	2.413 ± 1.019
Total	90	4.112± 1.835

Table no. 26 shows outcome with mean Psoas muscle index (PMI) in study populations. The mean PMI in study population was 4.112 ± 1.835. It was significantly higher in Survived group (4.53 ± 1.74) than Expired group (2.413 ± 1.01) with P value being <0.001

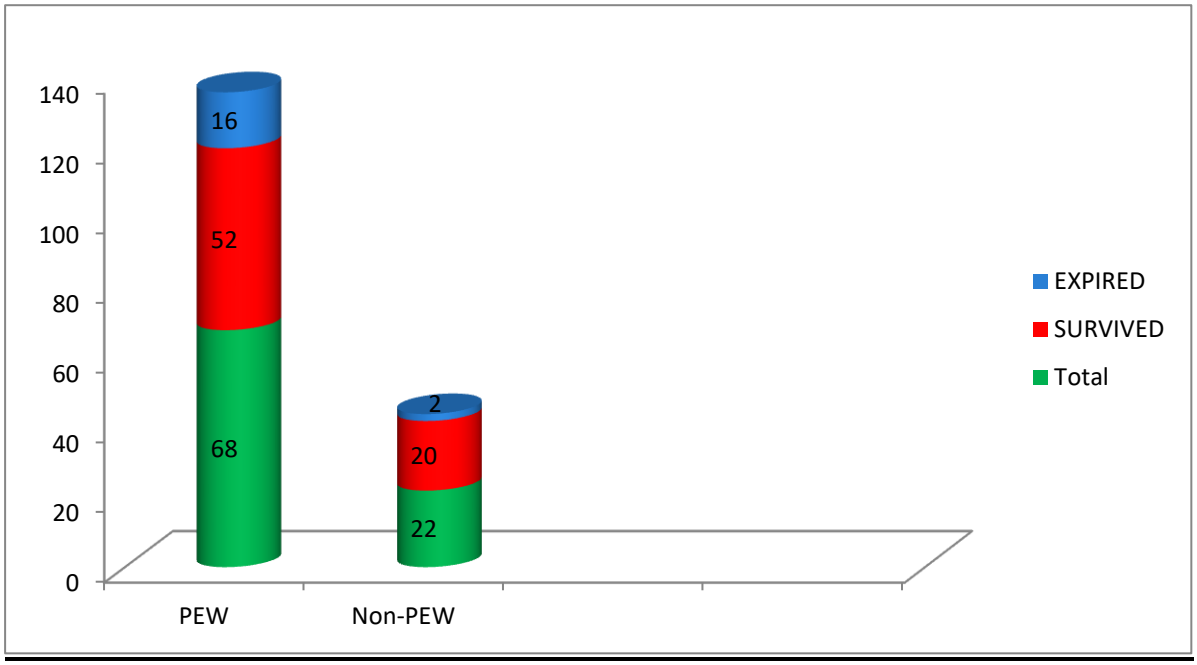
(P value < 0.0001) The mean of EXPIRED minus SURVIVED equals -2.123

Groups CKD	Number of Patients	PMI Mean ± SD
PEW	68	3.5228 ± 1.1949
Non-PEW	22	5.7273 ± 1.497
Total	90	4.112 ±1.835

Table no. 27 shows mean Psoas muscle index (PMI) in study populations between PEW and Non-PEW Group. The mean PMI in study population was 4.112 ±1.835. It was statically significant higher in Non-PEW group (5.7273 ± 1.497) than PEW group (3.5228 ± 1.1949) with P value being <0.001

Groups CKD	Number of patients Survived	Number of patients Expired	Total
PEW	52 (72.22%)	16 (88.8%)	68 (75.55%)
Non - PEW	20 (27.78%)	02 (11.2%)	22 (24.45%)
Total	72	18	90

Table no. 28 shows outcom in study populations between PEW and non- PEW Group. In our study prevalence of PEW was 75.55%. Mortality was significantly higher in PEW group (17.7 %) (p value being <0.001)



DISCUSSION

The present study was conducted to ascertain the association between PEW and Psoas muscle index in patients with CKD. In addition, this study also explore to find out prevalence of PEW in patients with CKD. This study also highlights the physical and clinical profile in CKD patients. 90 patients with CKD stage 3 to 5 + 5D were the study subjects in this study.

PMI has been evaluated in several clinical settings [76]; however, to date, few reports of dialysis patients have been published [81]. In this study, the PMI measurements using the MT method based on the abdomen-pelvic CT examination reflected the muscle mass status because of the significant positive association with physical parameters as BMI, MUAC and handgrip.

The psoas muscle was measured at only one cross-sectional area at the lower border of L3 level in this study Therefore, we checked whether PMI could be used as a. As a result, PMI calculated using the MT method significantly correlated with muscle mass and protein energy wasting (PEW)

The main findings of the our study were that CT-measured PMI was strongly associated with BMI , Handgrip ,MUAC and SGA which were markers of protein energy wasting, and that a low PMI was independently associated with an increased risk of all-cause and cardiovascular mortality in patients undergoing haemodialysis. Therefore, PMI may be an indicator of protein energy wasting and, consequently, a simple and useful tool for accurately predicting mortality in this population.

Recently, CT-measured PMTH has emerged as a marker of muscle wasting as well as a prognostic indicator of mortality in patients with liver disease [77]. Compared with conventional CT-based sarcopenic indices measured at the L3 level, this novel method has advantages such as no requirement of specific software or technical skills. However, it also has some issues that need to be addressed before it is standardized for use. Durand et al.and Huguet et al. reported that CT-measured PMI at the umbilicus level predicts mortality in patients with liver cirrhosis.

The mean age of our study population was 51.81±14.61 years with maximum number of patients (26.6%) in the age groups 51-60 yrs. This is in accordance with a similar study by Byung Hoon Kwack et al.[85] (2021) in south korea

The most common syndromic diagnosis in CKD patients was CTIN (81.12%) than CGN.

In our study in CTIN group most common etiology was obstructive uropathy, although in previous study most frequent cause of obstructive uropathy is prostatic hyperplasia but in our study the cause was Renal stone disease (RSD) due to inclusion criteria limitations.

In our study, the prevalence of Protein Energy Wasting (PEW) using biochemical and physical parameters was 75.55%, similar prevalence also found in previous study but the limitations regarding the small sample size and the cross-sectional design without sample size calculation according to the hypothesis

In the study population with PEW group the mean PMI was 3.5228 ± 1.1949 cm^2/m^2
Which was lower than Non-PEW group 5.7273 ± 1.497 cm^2/m^2 (statistically significant P Value <0.001). Similar to our study, Takahiro Yajima et al. [86] obtained correlation of PMI/PMTH with muscle wasting and geriatric nutritional risk index (GNRI).

In our study, PMI value <2.0 cm^2/m^2 was associated with higher mortality and more muscle wasting than PMI > 2.5 cm^2/m^2, although there is no specified PMI cut-off value proposed but similar study done by Ryo Kasahara et. al. [95] they use PMI cut-off in survival and expired patients.

In our study, lower PMI associated with mortality. In expired group mean PMI was 2.413 ± 1.019 cm^2/m^2 compared to survived group PMI was 4.53 ± 1.749 $cm^2/m^{2.}$.Similar to our study., Takahiro Yajima et al. [86] found higher mortality with lower PMI value.

Morrell GR et al. [81] also obtained similar association between PMI and mortality in patients with CKD. Kurumisawa S et al [13].also found strong association between Low PMI with higher mortality in dialysis patients. Takamoto D et al., obtained similar result in term of PMI and mortality in patients with CKD.

In our study ,the mean PMI was 4.112 ± 1.835 cm^2/m^2 which was lower than normal population. Similar to our study, Kiyonori Ito et al. [84] found the PMI was 4.79 ± 1.61 cm^2/m^2 in study population.

In our study Psoas Muscle Index (PMI) was positively correlate with Body Mass Index (BMI), Mid

Upper Arm Circumference (MUAC), Subjective Global Assessment (SGA)And Handgrip, correlation of PMI with BMI, MUAC, SGA and Handgrip was statistically significant
(P value < .01). Similar to Our study, Byung Hoon Kwack et al. [85] obtained significant correlation of Psoas Muscle index with BMI, SGA and Handgrip.

In our study Psoas Muscle Index (PMI) was statistically significant between Male and Female group. PMI was higher in Male population 4.512 ± 1.929 than Female population 3.228 ± 1.231 which was significant (P Value <0.05). Similar to our study, Kiyonori Ito et al. [84] found PMI higher in Male group in comparison to Female group.

In our study, Handgrip strength in term of sex and specified age group was lower than normal population, study done by Prachita Walankar et al. [96] (2016) in India in term of sex and specified age group.

In our study, PMI value was positively and significantly associated with Physical parameters as BMI, MUAC and Handgrip strength. PMI value significantly correlated with SGA and biochemical parameters as Cholesterol and Albumin. Although our study was cross-sectional but we evaluated PMI and patient prognosis because patients were in regular follow-up in our centre during study period from January 2020 to December 2021 and outcome was significantly associated with PMI value.In expired group PMI value was significantly lower than survived group

Our study has inherent limitations, including a cross-sectional design with a single-center setting and a small number of patients. The sample size was very small, and therefore, we could not evaluate PMI by gender-specific muscle.

Second, we did not use the measurement software which could automatically analyze the psoas muscle, therefore it might be possible to include the measurement error in PMI values due to the errors derived manually in this study.

In conclusion, the present study suggested that the Psoas Muscle Index (PMI) may be applicable as an early and useful indicator for detecting muscle strength and physical performance among CKD

patients. Therefore, PMI may be an indicator of protein energy wasting and could be considered a simple and useful tool for accurately predicting mortality in this population. Similar to our study Kiyonori Ito et al. [84] obtained strong association between PMI and skeletal Muscle Index (SMI) and poor patient prognosis therefore PMI may be consider as a tool to detect early malnutrition in CKD patients to apply of early interventions for better outcome because SMI calculation is cumbersome and SMI is affected by multiple factors as exercise .In our study PMI value is significantly associated with physical and biochemical parameters as well as mortality, therefore PMI can be used as a marker of malnutrition and muscle wasting and to predict outcome in CKD patients specially undergoing dialysis.

SUMMARY AND CONCLUSION

The present study was conducted in the Department of Nephrology in collaboration with Department of Radiodiagnosis, All India Institute of Medical Sciences (AIIMS), Jodhpur. The study was planned to evaluate the magnitude of association between Psoas Muscle Index (PMI) and Protein Muscle Wasting (PEW) in patients with chronic kidney disease (CKD). Ninety (90) patients with CKD stage 3 to 5 + 5D were taken as the study subjects when CT scans are performed for reasons other than to measure muscle mass. No control group was used.

This was observational and cross-sectional study which done from January 2020 to December 2021. In our study PEW was diagnosed on the basis of anthropometric and biochemical parameters. Different anthropometric parameters as Weight, Height, Body Mass Index (BMI), MAUC, Handgrip and SGA were used. Diagnostic biochemical tests as Creatinine, Urea, Serum Albumin, Serum cholesterol PTH were done.

The following results were obtained:

- The mean age of our study population was 51.81±14.61 years with maximum number of patients (26.6%) in the age groups 51-60 yrs. In the study there were more males (68.9%) as compared females (31.9%) in this study and the M: F ratio was 2.21.

- In our study mean age in CTIN group was 53.92 ± 14.11yrs as compared to CGN group 41.26 ± 12.75 yrs. In study population mean age was more in Female54.71 ± 15.93 as compared Male patients 50.5 ± 13.9 yrs.

- In syndromic diagnosis more patients were in CTIN group (81.12%) than CGN group (18.88%). In CTIN group most common etiology was obstructive uropathy 61 out of 73 patients (83.56%).

- In our study mean value of BMI was 19.84 ± 3.19 with minimum and maximum value was 13.14 and 25.92 kg/m2 respectively.

- Mean GFR in study population was 19.60 ± 14.081 with maximum and minimum GFR was 3 & 58 ml/min/BSA.

- In our study populations maximum patients (72.22%) were moderate to severely malnourished with using SGA 7-point score with maximum number of patients (65) in SGA category 3-5 score.

- In our study mean value of Psoas Muscle Index (PMI) was 4.112 ± 1.835 cm^2/m^2 .PMI value was more in Male group 4.512 ± 1.929 cm^2/m^2 as compared Female group 3.228 ± 1.231 cm^2/m^2 which was statistically significant (p value < 0.01).

- In our study mean value of Psoas Muscle Index (PMI) in CGN group 7.50 ± 0.422 cm^2/m^2 was more than CTIN group 3.498 ± 1.200 cm^2/m^2 which was statistically significant (p value < 0.01)

- In our study 64 patients (71.1%) received renal replacement therapy including Haemodialysis (62 patient) and Peritoneal dialysis (2 patients)

- In our study Psoas Muscle Index (PMI) was strongly correlate with anthropometric parameters as BMI, SGA, Handgrip and MUAC by using Pearson correlation formula and the result was statistically significant.

- In our study Psoas Muscle Index (PMI) was correlate with biochemical parameters as cholesterol and serum albumin but it was weak association with serum PTH.

- In our study Prevalence of Protein Muscle Wasting (PEW) was in 75.55% study population.

- In PEW group mean PMI was 3.5228 ± 1.1949 cm^2/m^2 which was lower than Non-PEW group 5.7273 ± 1.497 cm^2/m^2 and result was statistically significant.

- In our study population mortality was 20% and mean PMI was 2.413 ± 1.019 cm^2/m^2 which was lower than in survived group 4.53 ± 1.749 cm^2/m^2 which was statistically significant.

- In PEW group mortality was 88.8% as compared in Non-PEW group in which was 11.2%.

BIBILIOGRAPHY

1.KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease.2012; 2(4)

2.Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr.1997; 127(5Suppl):990S–991S.

3. Hung WW, Ross JS, Boockvar KS, Siu AL. Recent trends in chronic disease, impairment and disability among older adults in the United States. BMC Geriatric. 2011; 11:47 [PubMed: 9164280

4.Qureshi AR,Alvestrand A,Danielsson A et al. Factors predicting malnutrition in hemodialysis patients: a cross-sectional study. Kidney Int 1998; 53:773-82.

5. Carrero JJ, Stenvinkel P, Cuppari L, Ikizler TA, Kalantar-Zadeh K, Kaysen G, Mitch WE, Price SR, Wanner C, Wang AY, ter Wee P, et al. Etiology of the protein-energy wasting syndrome in chronic kidney disease: A consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM) J Ren Nutr. 2013;23(2):77–90. A consensus statement for the etiology of PEW in CKD from the ISRNM.

6. Sabatino, A., Cuppari, L., Stenvinkel, P., Lindholm, B. & Avesani, C. M. Sarcopenia in chronic kidney disease: What have we learned so far?. J. Nephrol. 2020;10.1007/s40620-020-00840-y

7. Tangvoraphonkchai, K. & Davenport, A. Changes in body composition following haemodialysis as assessed by bioimpedance spectroscopy. Eur. J. Clin. Nutr. 2017 ;71, 169–172.

8. Shachar, S. S., Williams, G. R., Muss, H. B. & Nishijima, T. F. Prognostic value of sarcopenia in adults with solid tumours: A metaanalysis and systematic review. Eur. J. Cancer.2016; 57, 58–67.

9.Amini, B., Boyle, S. P., Boutin, R. D. & Lenchik, L. Approaches to assessment of muscle mass and myosteatosis on computed tomography: A systematic review. J. Gerontol. A. Biol. Sci. Med. Sci.2019; 74, 1671–1678.

10. Huguet, A. et al. Te psoas muscle transversal diameter predicts mortality in patients with cirrhosis on a waiting list for liver transplantation: A retrospective cohort study. Nutrition 2018 ;51–52, 73–79 .

11. Paternostro, R. et al. Te value of diferent CT-based methods for diagnosing low muscle mass and predicting mortality in patients with cirrhosis. Liver. Int. 2019 ;39, 2374–2385.

12. Fukasawa, H. et al. Lower thigh muscle mass is associated with all-cause and cardiovascular mortality in elderly hemodialysis patients. Eur. J. Clin. Nutr.2017; 71, 64–69.

13. Kurumisawa, S. & Kawahito, K. Te psoas muscle index as a predictor of long-term survival after cardiac surgery for hemodialysisdependent patients. J. Artif. Organs 2019; **22**, 214–221.

14.Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-Analysis. PLoS One 2016;11:-0158765.

15.Kopple JD. McCollum Award Lecture, 1996: protein-energy malnutrition in maintenance dialysis patients. [Review] [134 refs]. Am J Clin Nutr 1997;65:1544-57.

16.Lindholm B, Heimburger O, Stenvinkel P. What are the causes of protein-energy malnutrition in chronic renal insufficiency? Am J Kidney Dis 2002;39:422-5.

17.Rambod M, Bross R, Zitterkoph J, et al. Association of Malnutrition-Inflammation Score With Quality of Life and Mortality in Hemodialysis Patients: A 5-Year Prospective Cohort Study. Am J Kidney Dis 2008.

18.Stenvinkel P, Heimburger O, Paultre F, et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney Int 1999;55:1899-911.

19. Carrero JJ, Stenvinkel P, Cuppari L, et al. Etiology of the protein-energy wasting syndrome in chronic kidney disease: a consensus statement from the International Society of Renal Nutrition and Metabolism (ISRNM). J Ren Nutr. 2013;23:77-90.

20. Ikizler TA, Cano NJ, Franch H, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. Kidney Int. 2013;84:1096-1107.

21.Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, Franch H, Guarnieri G, Ikizler TA, Kaysen G, Lindholm B, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. Kidney Int. 2008;73(4):391–398.

22. Mamoun AH, Sodersten P, Anderstam B, Bergstrom J. Evidence of splanchnic-brain signaling in inhibition of ingestive behavior by middle molecules. J Am Soc Nephrol 1999; 10:309-14.

23. Ikizler TA, Greene JH, Wingard RL, et al. Spontaneous dietary protein intake during progression of chronic renal failure. J Am Soc Nephrol 1995;6:1386-91.

24.Cohen SD, Kimmel PL. Nutritional status, psychological issues and survival in hemodialysis patients. Contrib Nephrol 2007; 155:1-17.

25. Van VB, Schoonjans R, Vanholder R, et al. Dyspepsia and gastric emptying in chronic renal failure patients. Clin Nephrol 2001; 56:302-7.

26. Silang R, Regalado M, Cheng TH, Wesson DE. Prokinetic agents increase plasma albumin in hypo-albuminemic chronic dialysis patients with delayed gastric emptying. Am J Kidney Dis 2001;37:287-93.

27.Wren AM, Seal LJ, Cohen MA, et al. Ghrelin enhances appetite and increases food intake in humans. J Clin Endocrinol Metab 2001;86:5992.

28. Yoshimoto A, Mori K, Sugawara A, et al. Plasma ghrelin and desacyl ghrelin concentrations in renal failure. J Am Soc Nephrol 2002;13:2748-52.

29. Wynne K, Giannitsopoulou K, Small CJ, et al. Subcutaneous ghrelin enhances acute food intake in malnourished patients who receive maintenance peritoneal dialysis: a randomized, placebo-controlled trial. J Am Soc Nephrol 2005;16:2111-8.

30. Perez-Fontan M, Cordido F, Rodriguez-Carmona A, et al. Shortterm regulation of peptide YY secretion by a mixed meal or peritoneal glucose-based dialysate in patients with chronic renal failure. Nephrol Dial Transplant 2008;23:3696-703.

31. DeFronzo RA, Alvestrand A, Smith D, et al. Insulin resistance in uremia. Journal of Clinical Investigation 1981;67:563-8.

32. Siew ED, Pupim LB, Majchrzak KM, et al. Insulin resistance is associated with skeletal muscle protein breakdown in non-diabetic chronic hemodialysis patients. Kidney Int 2007;71: 146-52.
33. Ding H, Gao XL, Hirschberg R, et al. Impaired actions of insulin-like growth factor 1 on protein synthesis and degradation in skeletal muscle of rats with chronic renal failure. Evidence for a post receptor defect. J Clin Invest 1996;97: 1064-75.

34. Zhang L, Wang XH, Wang H, et al. Satellite cell dysfunction and impaired IGF-1 signaling cause CKD-induced muscle atrophy. J Am Soc Nephrol 2010;21:419-27.

35. Brunelli SM, Thadhani R, Ikizler TA, Feldman HI. Thiazolidinedione use is associated with better survival in hemodialysis patients with non-insulin dependent diabetes. Kidney Int 2009;75:961-8.

36. Rabkin R, Sun DF, Chen Y, et al. Growth hormone resistance in uremia, a role for impaired JAK/STAT signaling. Pediatr Nephrol 2005;20:313-8.

37.Feldt-Rasmussen B, Lange M, Sulowicz W, et al. Growth hormone treatment during hemodialysis in a randomized trial improves nutrition, quality of life, and cardiovascular risk. J Am Soc Nephrol 2007;18:2161-71.

38. Carrero JJ, Qureshi AR, Parini P, et al. Low serum testosterone increases mortality risk among male dialysis patients. J Am Soc Nephrol 2009;20:613-20.

39. Menon V, Wang X, Greene T, et al. Factors associated with serum leptin in patients with chronic kidney disease. Clin Nephrol 2004;61:163-9.

40. Stenvinkel P, Lindholm B, Lonnqvist F, et al. Increases in serum leptin levels during peritoneal dialysis are associated with inflammation and a decrease in lean body mass. J Am Soc Nephrol 2000;11:1303-9.

41. Zoccali C, Mallamaci F, Tripepi G, et al. Adiponectin, metabolic risk factors, and cardiovascular events among patients with endstage renal disease. J Am Soc Nephrol 2002;13:134-41

42. Cheng LT, Tang W, Wang T. Strong association between volume status and nutritional status in peritoneal dialysis patients. Am J Kidney Dis 2005;45:891-902.

43. Paniagua R, Ventura MD, Avila-Diaz M, et al. NT-proBNP, fluid volume overload and dialysis modality are independent predictors of mortality in ESRD patients. Nephrol Dial Transplant 2010;25:551-7.

44. Wu DY, Shinaberger CS, Regidor DL, et al. Association between serum bicarbonate and death in hemodialysis patients: is it better to be acidotic or alkalotic? Clin J Am Soc Nephrol 2006;1:70-8.

45. de Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. J Am Soc Nephrol 2009;20:2075-84.

46.Mehrotra R, Bross R, Wang H, et al. Effect of high-normal compared with low-normal arterial pH on protein balances in automated peritoneal dialysis patients. Am J Clin Nutr 2009; 90:1532-40.

47. Raj DS, Sun Y, Tzamaloukas AH. Hypercatabolism in dialysis patients. Curr Opin Nephrol Hypertens 2008;17:589-94.

48. Boivin MA, Battah SI, Dominic EA, et al. Activation of caspase-3 in the skeletal muscle during haemodialysis. Eur J Clin Invest 2010;40:903-10.

49. Song YH, Li Y, Du J, et al. Muscle-specific expression of IGF-1 blocks angiotensin II-induced skeletal muscle wasting. J Clin Invest 2005;115:451-8
.
50. Raj DS, Boivin MA, Dominic EA, et al. Haemodialysis induces mitochondrial dysfunction and apoptosis. Eur J Clin Invest 2007;37:971-7.

51. Mitch WE. Robert H Herman Memorial Award in Clinical Nutrition Lecture, 1997. Mechanisms causing loss of lean body mass in kidney disease. Am J Clin Nutr1998;67:359-66.

52. Kopple JD, Bernard D, Messana J, et al. Treatment of malnourished CAPD patients with an amino acid based dialysate. Kidney Int 1995;47:1148-57.

53. Workeneh BT, Rondon-Berrios H, Zhang L, Hu Z, Ayehu G, Ferrando A, et al. Development of a diagnostic method for detecting increased muscle protein degradation in patients with catabolic conditions. J Am Soc Nephrol 2006;**17**(11):3233–9.

54.Degoulet P, et al. Mortality risk factors in patients treated by chronic hemodialysis. Report of the Diaphane collaborative study. Nephron. 1982;31(2):103-110.

55. Fleischmann E, et al. Influence of excess weight on mortality and hospital stay in 1346 hemodialysis patients. Kidney Int. 1999;55(4):1560-1567.

56. Kopple JD, et al. Body weight-for-height relationships predict mortality in maintenance hemodialysis patients. Kidney Int. 1999;56(3):1136-1148.

57. Wolfe RA, et al. Body size, dose of hemodialysis, and mortality. Am J Kidney Dis. 2000;35(1):80-88.

58. Leavey SF, et al. Body mass index and mortality in 'healthier' as compared with 'sicker' haemodialysis patients: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2001;16(12):2386-2394.

59. Port FK, et al. Dialysis dose and body mass index are strongly associated with survival in hemodialysis patients. J Am Soc Nephrol. 2002;13(4):1061-1066.

60. Lowrie EG, et al. Body size, dialysis dose and death risk relationships among hemodialysis patients. Kidney Int. 2002;62(5):1891-1897.

61. Glanton CW, et al. Factors associated with improved short term survival in obese end stage renal disease patients. Ann Epidemiol. 2003;13(2):136-143.

62. Johansen KL, et al. Association of body size with outcomes among patients beginning dialysis. Am J Clin Nutr. 2004;80(2): 324-332.

63. Kalantar-Zadeh K, et al. Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. Am J Kidney Dis. 2005;46(3): 489-500.

64. Kalantar -Zadeh K, et al. Mortality prediction by surrogates of body composition: an examination of the obesity paradox in hemodialysis patients using composite ranking score analysis. Am J Epidemiol. 2012;175(8):793-803.

65. Park J, et al. Mortality predictability of body size and muscle mass surrogates in Asian vs white and African American hemodialysis patients. Mayo Clin Proc. 2013;88(5): 479-486.

66. Pereira RA, Cordeiro AC, Avesani CM, et al. Sarcopenia in chronic kidney disease on conservative therapy: prevalence and association with mortality. Nephrol Dial Transplant 2015; 30:1718–1725.

67. Zhou Y, Hellberg M, Svensson P, et al. Sarcopenia and relationships between muscle mass, measured glomerular filtration rate and physical function in patients with chronic kidney disease stages 3–5. Nephrol Dial Transplant 2018; 33:342–348.

68. Lee SJ, Son H, Shin SK. Influence of frailty on health-related quality of life in predialysis patients with chronic kidney disease in Korea: a cross-sectional study. Health Qual Life Outcomes 2015; 13:1–7.

69. Roshanravan B, Khatri M, Robinson-Cohen C, et al. A prospective study of frailty in nephrology-referred patients with CKD. Am J Kidney Dis 2012; 60:912–921.

70. Isoyama N, Qureshi AR, Avesani CM, et al. Comparative associations of muscle mass and muscle strength with mortality in dialysis patients. Clin J Am Soc Nephrol 2014; 9:1720 1728.

71. Kim JK, Choi SR, Choi MJ, et al. Prevalence of and factors associated with sarcopenia in elderly patients with end-stage renal disease. Clin Nutr 2014; 33:64–68.

72. Ren H, Gong D, Jia F, et al. Sarcopenia in patients undergoing maintenance hemodialysis: incidence rate, risk factors and its effect on survival risk. Ren Fail 2016; 38:364–371.

73. Bataille S, Serveaux M, Carreno E, et al. The diagnosis of sarcopenia is mainly driven by muscle mass in hemodialysis patients. Clin Nutr 2017; 36:1654–1660.

74. Marini ACB, Perez DRS, Fleuri JA, Pimentel GD. SARC-F is better correlated with muscle function indicators than muscle mass in older hemodialysis patients. J Nutr Heal Aging 2020; 24:999–1002.

75. Lin YL, Liou HH, Wang CH, et al. Impact of sarcopenia and its diagnostic criteria on hospitalization and mortality in chronic hemodialysis patients: A 3- year longitudinal study. J Formos Med Assoc 2020; 119:1219–1229.

76.Okamura H, Kimura N, Tanno K, Mieno M, Matsumoto H, Yamaguchi A, et al. The impact of preoperative sarcopenia, defined based on psoas muscle area, on long-term outcomes of heart valve surgery. J Thorac Cardiovasc Surg 2018;157:1071

77.Dae Hoe Gu, Moon Young Kimet al. Clinical usefulness of psoas muscle thickness for the diagnosis of sarcopenia in patients with liver cirrhosis. Clinical and Molecular Hepatology 2018;24:319-330

78.Ranjani N. Moorthi & Keith G. Avin et al. Clinical relevance of sarcopenia in chronic kidney disease. Curr Opin Nephrol Hypertens. 2017 May; 26(3): 219–228

79.Jukes P.Namm et al. A semi-automated assessment of sarcopenia using psoas area and density predicts outcomes after pancreaticoduodenectomy for pancreatic malignancy. Journal of Gastrointestinal Oncology 8(6):936-94

80.Noriko Ishii , Yoshinori Iwata , Hiroki Nishikawa et al. Effect of pre-treatment psoas muscle mass on survival for patients with unresectable pancreatic cancer undergoing systemic chemotherapy. Oncol Lett. 2017 Nov; 14(5): 6059–6065

81 Morrell GR, Ikizler TA, Chen X, Heilbrun ME, Wei G, Boucher R, et al. Psoas muscle cross-sectional area as a measure of whole-body lean muscle mass in maintenance hemodialysis patients. J Ren Nutr 2016;26:258e64.

82.Kazuhiro Harada MD , Susumu Suzuki, MD, Hideki Ishii et al. Impact of Skeletal Muscle Mass on Long-Term Adverse Cardiovascular Outcomes in Patients With Chronic Kidney Disease.doi.org/10.1016/j.amjcard.2017.01.003

83.Alice Sabatino, Claudia D'Alessandro et al. Muscle mass assessment in renal disease: the role of imaging techniques. doi: 10.21037/qims.2020.03.05

84.Kiyonori Ito , Susumu Ookawara , Sojiro Imai et al. Muscle mass evaluation using psoas muscle mass index by computed tomography imaging in hemodialysis patients.Clinical Nutrition ESPEN 44 (2021) 410-414.

85.Byung Hoon Kwack, Jun Chul Kim, Jun Young Do ,Seok Hui Kang, et al. Association Between the Normal-Density Psoas Muscle Index and Handgrip Strength or Gait Speed in Maintenance Hemodialysis Patients. BRIEF RESEARCH REPORT published: 28 July 2021 doi: 10.3389/fmed.2021.712497

86.TakahiroYajima, MaikoArao , KumikoYajima & HiroshiTakahashi et al. Usefulness of computed tomography-measured psoas muscle thickness per height for predicting mortality in patients undergoing hemodialysis. Scientific Reports | (2021) 11:19070

87.Kosei Yamaguchi, Mineaki Kitamura, Takahiro Takazono, Shuntaro Sato et al. Association between the psoas muscle index and hospitalization for pneumonia in patients undergoing hemodialysis. BMC Nephrology (2021) 22:394

88. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol 1996; 7: 198–207

89. Talke, H. and Schubert, G.E., Klinische Wochenschrift, 1965;43: 174.

90.Gitelman HJ. An improved automated procedure for the determination of calcium in biochemical specimen. Anal. Biochem 1967;18: 521-531.

91.Daly JA, Ertingshausen G. Direct method for determining inorganic phosphate in serum with the "CentrifiChem". Clin Chem 1972;18(3):263-5.

92.Weichselbaum TE. An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. Amer J Clin Path 1946; 16:40-48

93.Doumas BT, Watson WA, Biggs HG. Albumin standards and the measurement of serum albumin with bromcresol green. Clin Chim Acta 1971;31:87-96.

94.Habener JF, Segre GV 1979 Parathyroid Hormone Radioimmunoassay, Annals of Internal Medicine 91, 782.

95.Ryo Kasahara, Takashi Kawahara et al. A Low Psoas Muscle Index before Treatment Can Predict a Poorer Prognosis in Advanced Bladder Cancer Patients Who Receive Gemcitabine and Nedaplatin Therapy. Hindawi BioMed Research International Volume 2017, Article ID 7981549

96.Prachita Walankar , Chhaya Verma et al. Study of Hand Grip Strength in Indian Population. International Journal of Health Sciences and Research ISSN: 2249-9571

ANNEXURE-1

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2020/3117 **Date: 01/01/2020**

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/**1636

Project title: **"Study of the association between protein energy wasting (PEW) and psoas muscle index (PMI) in patients with CKD."**

Nature of Project:	**Research Project**
Submitted as:	**D.M. Dissertation**
Student Name:	**Dr.Mahendra Kumar Jangid**
Guide:	**Dr.Manish Chaturvedy**
Co-Guide:	**Dr. Praveen Sharma, Dr.Nitin Kumar Bajpai & Dr.Pawan Kumar Garg**

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **17-01-2020** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary
Institutional Ethics Committee
AIIMS,Jodhpur

Enclose:
1. Annexure 1

Basni Phase-2, Jodhpur, Rajasthan-342005, Website: www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
Email: ethicscommittee@aiimsjodhpur.edu.in

Annexure I

Institutional Ethics Committee
All India Institution of Medical Sciences, Jodhpur

Meeting of Institutional Ethics committee held on **17-01-2020 at 10:00** AM at Committee Room, Admin Block AIIMS Jodhpur.

Following members were participated in the meeting:-

S/No.	Name of Member	Qualification	Role/Designation in Ethics Committee
1.	Dr. F.S.K Barar	MBBS, MD (Pharmacology)	**Chairman**
2.	Justice N.N Mathur	LLB	Legal Expert
3.	Dr. Varsha Sharma	M.A (Sociology)	Social Scientist
4.	Mr. B.S.Yadav	B.Sc., M.Sc. (Physics), B.Ed.	Lay Person
5.	Dr. K.R.Haldiya	MD (General Medicine)	Clinician
6.	Dr. Arvind Mathur	MBBS, MS (General Medicine)	Clinician
7.	Dr. Sneha Ambwani	MBBS, MD (Pharmacology)	Basic Medical Scientist
8.	Dr. Kuldeep Singh	MBBS, MD (Paediatric), DM (General Medicine)	Clinician
9.	Dr. Abhinav Dixit	MBBS, MD (Physiology), DNB (Physiology)	Basic Medical Scientist
10.	Dr. Pradeep Kumar Bhatia	MBBS, MD (Anaesthesiology)	Clinician
11.	Dr. Tanuj Kanchan	MBBS, MD (Forensic Medicine)	Basic Medical Scientist
12.	Dr. Pankaj Bhardwaj	MBBS, MD (CM&FM)	Clinician
13.	Dr. Praveen Sharma	M.Sc., Ph.D. (Biochemistry)	Member Secretary

Dr. Praveen Sharma
Member Secretary
Institutional Ethics Committee
AIIMS,Jodhpur

ANNEXURE-2

All India Institute of Medical Sciences, Jodhpur, Rajasthan

INFORMED CONSENT FORM

I _____ S/o or D/o_____

R/o _____ hereby declare that I give informed consent to participate in the Thesis study labelled **"STUDY OF THE ASSOCIATION BETWEEN PROTEIN ENERGY WASTING (PEW) AND PSOAS MUSCLE INDEX (PMI) IN PATIENTS WITH CKD".** Dr.Mahendra kumar Jangid has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various investigations to be carried out for the study. I have been informed about the duration of the study and possible complications caused by study.

I give full consent for being enrolled in the above study and I reserve my rights to withdraw from the study whenever I wish without prejudice of my right to undergo further treatment at this hospital and its associated hospitals.

_____ _____

Name of Subject Date Signature of subject

We have witnessed that the patient signed the above form in the presence of his/her free will after fully having understood its contents.

_____ _____

Name of Witness Date Signature of witness

_____ _____

Name of Investigator Date Signature of Investigator

ANNEXURE-3

अखिल भारतीय आयुर्विज्ञान संस्थान

जोधपुर, राजस्थान

सूचित सहमति प्रपत्र

थीसिसकाशीर्षक 'क्रोनिक किडनी रोग के रोगियों में प्रोटीन ऊर्जा बर्बाद करने और पेसो मांसपेशी सूचकांक के बीच संबंध का अध्ययन करें द्वाराडॉ. महेंद्रकुमारजांगिड़

रोगी / स्वयंसेवी पहचान संख्या.: _____

मैं,_____पुत्र/पुत्री_____

निवासी_____मेरीपूर्ण, निः शुल्क, स्वैच्छिक सहमति देता हु निम्नलिखित अध्ययन का हिस्सा बनने के लिए क्रोनिक किडनी रोग के रोगियों में प्रोटीन ऊर्जा बर्बाद करने और पेसो मांसपेशी सूचकांक के बीच संबंध का अध्ययन करें जिसकी प्रक्रिया और प्रकृति मेरी पूरी संतुष्टि के,किसी भी समय अध्ययन सेबाहर निकलने के मेरे अधिकार से अवगत हूं.मैं समझता हूं कि मेरे और मेरे किसी भी मेडिकल रिकॉर्ड के बारे में एकत्र की गई जानकारी एम्स जोधपुर सेयानियाम प्राधिकरणों सेजिम्मेदार व्यक्ति द्वारा देखी जा सकती है।मैं इन व्यक्तियों के लिए अपने रिकॉर्ड तक पहुंचने की अनुमति देताहूं ।

दिनांकः _____ _____

स्थान : _____ हस्ताक्षर/बाएंअंगूठेकीछाप

तारीख :_____ _____

स्थानः _____ हस्ताक्षर

यह प्रमाणित करने के लिए कि उपर्युक्त सहमति मेरी उपस्थिति में प्राप्त की गई है।

साक्षी1 साक्षी2

हस्ताक्षरः _____ हस्ताक्षरः _____

नामः _____ नामः _____

स्थान : _____ स्थान : _____

ANNEXURE- 4
PATIENT INFORMATION SHEET

Name of the patient: **Patient ID.:**

"STUDY OF THE ASSOCIATION BETWEEN PROTEIN ENERGY WASTING (PEW) AND PSOAS MUSCLE INDEX (PMI) IN PATIENTS WITH CKD".

1. **Aim of the study**:
   - To study the association between Protein Energy Wasting (PEW) and Psoas Muscle Index (PMI) in patients with CKD.
   - To identify magnitude of correlation of PEW using biochemical and anthropometric parameters with PMI as a tool to detect PEW.
2. **Study site:** Out Patient and in-patient services of Department of Nephrology, All India Institute of Medical Sciences, Jodhpur, Rajasthan.
3. **Study procedure:** After detailed history, clinical examination and necessary baseline laboratory investigations, patients will be diagnosed as PMTH- sarcopenia. Timely clinical and laboratory monitoring will be done.
4. **Likely benefit:** Study will help to know the causes of PEW and it's correlation with disease progression and morbidity.
5. **Confidentiality:** All the data collected from each study participant will be kept highly confidential.
6. **Risk:** Enrolment in above study poses no substantial risk to any of the study participant.
7. **Withdrawal from study**: You are free to decide whether to participate or not in the study or withdraw from the study anytime. If you choose not to participate in the study or withdraw from the study, you will continue to receive the same amount of care and treatment at AIIMS, Jodhpur.

ANNEXURE-5

रोगी सूचना पत्रक

रोगी का नाम: रोगी आईडी :

□क्रोनिक किडनी रोग के रोगियों में प्रोटीन ऊर्जा बर्बाद करने और सोआसमांसपेशी सूचकांक के बीच संबंध का अध्ययन करें□

अध्ययन का उद्देश्य:

1. प्रोटीन ऊर्जा बर्बाद करने का पता लगाने के लिए एक उपकरण के रूप में सोआसमांसपेशी सूचकांकबनाने के लिए

2. .क्रोनिक किडनी रोग के रोगियों में प्रोटीन ऊर्जा बर्बाद होने की व्यापकता का अध्ययन करने के लिए

3. अध्ययन साइट: नेफ्रोलॉजी विभाग, ऑल इंडिया इंस्टीट्यूट ऑफ मेडिकल साइंसेज, जोधपुर, राजस्थान।
4. गोपनीयता: प्रत्येक अध्ययन प्रतिभागी से एकत्र किए गए सभी डेटा को अत्यधिक गोपनीय रखा जाएगा।
4. अध्ययन से निकासी: आप यह तय करने के लिए स्वतंत्र हैं कि अध्ययन में भाग लेने या अध्ययन में या किसी भी समय अध्ययन से वापस लेना है या नहीं। यदि आप अध्ययन में भाग लेने या अध्ययन से वापस लेने का चयन नहीं करते हैं, तो आपको एम्स, जोधपुर में समान देखभाल और उपचार प्राप्त करना जारी रहेगा।

अधिक जानकारी / प्रश्नों के लिए, निम्नलिखित कर्मियों से संपर्क किया जा सकता है:
डॉ. महेंद्रकुमारजांगिड़, नेफ्रोलॉजी विभाग, ऑल इंडिया इंस्टीट्यूट ऑफ मेडिकल साइंसेज, जोधपुर, राजस्थान।
पीएच: 9140072180

ANNEXURE -6

PROFORMA

Name: Study Serial No.:

Age: Sex:

Reg No.:

Address: Phone No.:

Diagnosis:

Duration of CKD _____ eGFR (ml/min/BSA) _____

Weight (Kg.) _____ Height (cm.) _____ MUAC (cm.) _____ SGA_____

BMI (Kg/m^2) _____Handgrip (Kg.) _____

LABORATORY (BIOCHEMICAL)

Date	Baseline
Hb/TLC/PLT	
Na/K/Cl	
Urea /Cr	
SGOT/SGPT/ALP	
TP/ALB.	
CHOL/TRIGS	
Ca/Phos	
Vit D/PTH	

NCCT ABDOMEN to calculate PMI/PMTH_____