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Research Article

Prevalence of end stage renal disease in diabetic obese and hypertensive patients and cardiovascular risk in dialysis patients

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ABSTRACT

Chronic Kidney Disease (CKD) is cause of irreversible deterioration in renal function which leads to end stage renal disease (ESRD). Incidence of end-stage renal disease has increased dramatically during the last 30 years and screening for early stages of chronic kidney disease is often suggested as a preventive measure. The main causes of end stage renal disease are diabetes, high blood pressure, hyperlipidemia and obesity. Obesity and increased BMI are the cause of kidney stone and chronic kidney disease. This report aims to determine the prevalence of end stage renal disease in diabetic obese individuals and other problems that are more likely to be encountered in end stage renal disease are cardiovascular risks in dialysis patients. GFR and Creatinine clearance are used as major diagnostic tool to determine kidney function. Calcium level is also used as the predictive factor to determine the vascular calcification.

Keywords: Chronic kidney disease, ESRD, obesity, hypertension, GFR, creatinine clearance, cardiac vascular death

INTRODUCTION:

Chronic renal failure, or end stage renal disease, is a progressive and irreversible deterioration in renal function in which the body unable to maintain metabolic, fluid and electrolyte balance, resulting in retention of urea and other nitrogenous wastes in the blood. Chronic kidney disease (CKD) is permanent damage to the kidneys, if kidneys keep getting worse and can lead to kidney failure (ESRD) (Brimble *et al*, 2012).The most common causes of ESRD are diabetes, obesity, hypertension, cardiovascular diseases and smoking. ESRD almost always comes after chronic kidney disease (Gutiérrez *et al*, 2008).

Obesity

Excess weight is independent risk factor for end stage renal disease. Obesity is associated with increased insulin resistance and diabetes type 2 which is a major risk factor for ESRD(Siener et,2004; Hallan *et al*, 2006). The most common cause of end stage renal disease is the diabetes mellitus. The average expectancy life of diabetic dialysis patients is about five to six years. Because these are at the high risk of cardiovascular diseases. The dialyzed patients die due to cardiac disease before their kidney diseases become severe. This can be prevented by the strict hyperglycemic control. When oral antihyperglycemic therapy not suitable then insulin is the best therapeutic option in these patients.

Hypertension

It is one of the leading causes of chronic kidney disease due to the deleterious effects on kidney vasculature. Long-term, hypertension leads to high intra glomerular pressure, impairing

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glomerular filtration. Damage to the glomeruli lead to an increase in protein filtration, resulting in abnormally increased amounts of protein in the urine (micro albuminuria or proteinuria). Micro albuminuria is the presentation of small amounts of albumin in the urine and is often the first sign of chronic kidney disease. The relationship between chronic kidney disease and hypertension is cyclic, as chronic kidney disease can contribute to or cause hypertension. Elevated blood pressure leads to damage of blood vessels within the kidney, as well as throughout the body. This damage impairs the kidney's ability to filter fluid and waste from the blood, leading to an increase of fluid volume in the blood thus causing hypertension (Brow *et al*.,1971; Gao *et al* ,2004).Adequate blood pressure control is the most important factor for the preservation of renal function, so every drug that effectively lowers hypertension is believed to be renoprotective (Wright *et al*,2002). The reason for the prevalence of hypertension may be due to the inadequate dialysis. There is evidence that the blood pressure can be improved by long (more than 6 hours, slower dialysis time.

Vascular calcification

It is known to be a risk factor for ischemic heart disease in non-uremic individuals. Patients with end stage renal disease experience accelerated vascular calcification, due to dysregulation of mineral metabolism. Vascular calcification is a well-known complication of chronic kidney disease and one of the main predictors for increased cardiovascular morbidity and mortality in these patients. It may happen in two main types of intimal calcification, as a part of diffuse atherosclerosis, and medial calcification, which is generally focal in distribution, unrelated to atherosclerotic risk factors, and seen in younger hemodialysis patients. The extent of coronary calcification was more pronounced with older age male, gender, white race, diabetes, longer dialysis vintage and higher serum concentrations of calcium and phosphorus. Only dialysis vintage was significantly associated with the prevalence of vascular calcification (Bakris *et al*,2000) .

Cardiovascular disease is the major killer in end stage renal disease. Left ventricular abnormalities are present at initiation of dialysis in about 80% of dialysis patients (Foley and Parfery,2012). Chronic volume overload and anemia leading to left ventricular hypertrophy and altered the calcium-phosphate metabolism with vascular and coronary calcification contribute to the pathogenesis of IHD. Other risk factors that have been implicated include oxidative stress, homocysteine, and myocardial stunning while undergoing dialysis treatment. Additional risk factors include erythropoietin use for treating anemia, as well as use of calcium-based phosphate binders (Ariyamuthu *et al*,2012).

Hyperlipidemia

It is increased in patients having the chronic renal disease. In end stage renal disease patients, the low density lipoprotein level is high. Lipid lowering drugs should be given to these patients.

Others risk factors for the end stage renal disease are smoking which cause increase in blood pressure release of vasopressin and renovascular resistance.

PATHOPHYSIOLOGY

The basic pathophysiology of ESRD are Diabetes and hypertension leads to the loss of nephron mass which cause structural and functional hypertrophy of remnant nephrons. This causes the sclerosis of remnant nephrons and ultimately leads to further loss of nephron mass and permanent kidney damage (Coladonato, 2005). The prevalence of glomerular hyperfiltration increased with increasing stages of pre-diabetes and pre-hypertension, glomerular hyperfiltration leads to kidney damage (Taylor *et al*, 2005). Relationship between obesity and kidney disease increases. The

cause of renal damage due to obesity is not clearly defined. Hyperlipidemias, hyperfilteration, increased in sympathetic activity, increased activity of rennin angiotensin system are the contributing factors for the end stage renal disease. ESRD is more prevalent in diabetic patients. Diabetic nephropathy leads to RFD(renal function decline) and thus reduced GFRs and micro albuminuria and proteinuria which is the major diagnostic tool in determining the end stage renal disease stages (Pavkov *et al*, 2012; Taylor *et al*,2012).

The major problems detected in the End Stage Renal Disease were hypertension and the cardiovascular diseases. Cardiovascular death is the most frequent cause of dying in peritoneal dialysis (PD) patients. Hypertension is the most important general risk factor in PD patients, while obesity remains controversial. Inflammation, malnutrition, calcifications and probably endothelial dysfunction and oxidative stress are all cardiovascular risk factors present in ESRD that contribute to mortality in PD patients. Additional cardiovascular risk factors in PD are related to the glucose load, leading to increasing insulin resistance and a more atherogenic lipid profile. Loss of residual renal function and ultra filtration failure promote over hydration, which is the most important PD-related risk factor for cardio vascular disease (Harnett *et al*,1995).

EPIDEMOLOGY

30% approximately patients having Diabetic nephropathy progress to End-stage Renal failure and rest population usually die due to cardiovascular diseases before reach to End stage. All these have developed microalbuminuria and proteinuria. Albuminuria is the important risk factor in all these Patients. The diabetic patients must have to assess the microalbuminuria yearly. (Diabetic nephropathy. Diabetes Care, 2002) The renal diseases are strongly associated with albuminuria. The cardiovascular event are the prediction in the diabetic patients and also in the general population (Verhave *et al*,2002). So the patient having combination of hypertension, diabetes, and the chronic kidney diseases are now the most commonly cause of End-stage Kidney failure. In the year 1996, there were the 100 Patients/million populations beginning Dialysis in the Hong Kong. In 2000, this was increased to 122 Patients, and in the 2003, the 140 Patients/million population began treatments for End-stage Renal failure. Similarly, these rates have been increasing in United States, and with the increasing in prevalence, it is predicted that by the year 2010, this will be the almost 700,000. There is costing an about US$30 millions in year for the Dialysis treatments in United states**.** **(**Lysaght,2002) Obviously, the treatment of such is ever increasing the burden of End-stage renal failure cannot be afforded, even in wealthiest countries. In Hong Kong, renal Registry show progressive increase in number of diabetics beginning dialysis, which now represents 38% of incident in Patients, while the only 23% were due to the glomerulonephritis. In other countries throughout the Asia also have large percentage of their incidents End-stage renal failure Patients due to the diabetes: the Pakistan 42%, the Taiwan 35%, the Philippines 25% and the Japan 37% (USRDS 2003). It is also demonstrated that relatively the steady acceptance rate of Type 1 Diabetes over this time, but progressively increases in number of Type 2 Diabetic patients have been accepted into Dialysis program over past two decades. The diabetes is now major cause of End-stage renal failure world widely in the both developed countries and as well in the emerged countries.

The risk of cardiovascular disease in patients with chronic renal disease appears to be far greater than in the general population. For example, among patients treated by hemodialysis or peritoneal dialysis, the prevalence of coronary artery disease is approximately 40% and the prevalence of left ventricular hypertrophy is approximately 75%. Cardiovascular mortality has

been estimated to be approximately 9% per year. Even after stratification by age, gender, race, and the presence or absence of diabetes, cardiovascular mortality in dialysis patients is 10 to 20 times higher than in the general population. Patients with chronic renal disease should be considered in the highest risk group for subsequent cardiovascular events. Cardiac failure is more common in chronic renal disease patients than in the general population, and is an independent predictor of death in chronic renal disease. Among hemodialysis and peritoneal dialysis patients, the prevalence of cardiac failure is approximately 40%. Both coronary artery disease and left ventricular hypertrophy are risk factors for the development of cardiac failure. In practice, it is difficult to determine whether cardiac failure reflects left ventricular dysfunction or extracellular fluid volume overload. Patients who develop clinical manifestations of cardiac failure should be evaluated for cardiovascular disease.

Symptoms of ESRD:

A patient having ESRD may experience these symptoms:

- Decrease in urine output
- Difficulty to urinate
- Fatigue
- Headache
- Weight loss
- Appetite loss
- Nausea
- Vomiting
- Dry skin
- Itching
- Bone pain
- Skin color changed
- Numbness
- Excessive thirst
- frequent hiccups
- absence of menstrual cycles
- obstructive sleep apnea
- restless leg syndrome (RLS)
- low libido or impotence
- edema

DIAGNOSIS

To determine the prevalence of ESRD with different diseases various diagnostic tests are utilized to determine the RFD (renal function decline) in patients. Blood and urine samples are tested and radiographical imaging study techniques are utilized to diagnose and determine the stage of various comorbidities. The major diagnostic tool to determine the kidney function is GFR and creatinine clearance.

Glomerular filtration rate (GFR) Test

It is used to check how well the kidneys are working. Specifically, it estimates how much blood passes through the glomeruli each minute. Glomeruli are the tiny filters in the kidneys that filter waste from the blood. Increased GFR also called hyper filtration is a proposed mechanism for renal injury in several clinical conditions. A GFR of 120–149 mL/min/1.73 m^2 may be considered normal in Young adults (<30 years), in whom a level that exceeds 150 mL/min/1.73 m^2 may reflect hyperfiltration. Older people will have lower normal GFR levels, because GFR decreases with age. GFR of the 120–149 mL/min/ 1.73 m^2 may thus represent the hyperfiltration in elderly patients, whom have GFR of the 60-89 mL/min/1.73 m^2 is then considered normal.(Okada *et al*,2012) Levels below mL/min/1.73 m^2 for 3 or more months are a sign of chronic kidney disease. GFR result lower than 15 mL/min/1.73

m^2 is a sign of kidney failure requires immediate medical attention (Brimble *et al*, 2012).

Estimated glomerular filtration rate eGFR is determined by formula:

GFR (mL/min/1.73 m^2) = $175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times$ (0.742 if female) × (1.212 if African American)

The creatinine clearance Test

It involves a 24-hour urine collection, can also provide an estimate of kidney function. It is also major diagnostic tool of kidney function. The creatinine clearance test helps provide information about how well the kidneys are working. The test compares the creatinine level in urine with the creatinine level in blood. The normal creatinine level is 50-110µmol/L or 0.6-1.2mg/dL in serum and normal level of creatinine in urine in males is 8.8- 17.6µmol/L or 1.0-2.0 g/24h and in females is 7.0-15.8µmol/L or 0.8-1.8 g/24h. Decreased Creatinine clearance is marker of RFD (renal function decline) (Blacher *et al*, 1998).

It is calculated by various formulas as:

$CL_{(cr)} = (U \times V)/S$ (2)

Where; U= urine creatinine clearance (µmol/L) , V is the urine flow rate (mL/min) , S is the serum creatinine concentration (µmol/L).

The urine albumin-to-creatinine ratio

The albumin to creatinine ratio is determined between albumin and the creatinine level in urine. The Creatinine is waste material in blood which is filtered through the both kidneys and then excreted from the urine. Albumin Creatinine ratio (ACR) is more than 30mg is the indicator of chronic kidney disease (C O, 2012).

Normoalbuminuria = <30mg albumin/g Creatinine

Microalbuminuria =30 - 300 mg albumin/g Creatinine

Macroalbuminuria= > 300 mg/g Creatinine

The Dipstick test for albumin

The dipstick test is performed on urine sample which detect the presence of albumin in urine. Albumin is passed into urine when both kidneys are damaged. The urine samples of patient are collected in special container and then send it to lab for the analysis. For this test, a technician places a strip, called dipstick, into the urine sample. The patches on the dipstick change the color when there is protein or blood present in the urine. Albuminuria is marker of progression of CKD (Rao PK,,2008).

Renal ultrasound (sonography)

The sonography is used to determine the size and shape of kidney and also used to detect the mass, cyst, kidney stone, or any other obstruction or abnormalities.

Kidney biopsy

This procedure involves the removal of tissue samples (with a needle or during surgery) from the body for examination under a microscope; to determine if cancer or other abnormal cells are present (Mendelssohn D,1995).

Computed tomography scan (CAT scan)

A computed tomography scan shows the detail images of any part of body, including bones, fat, muscles and organs. The CT scans are more detailed than the general X-rays. The contrast CT cannot be done when there is renal failure. (Herman, G. T, 2009)

Histological examination of the arterial specimens

The gold standard for diagnosis of vascular calcification would be histological examination of the arterial specimens, which is not clinically feasible. The other recommended diagnostic techniques are electron beam computed

tomography, which is more of research interest and not accessible in most centers of the world; ultrasonographic measurement of pulse wave velocity or carotid intima-media thickness; and plain radiography of the abdominal aorta (Blacher *et al*, 1999; Persson *et al* ,1994; Kauppila *et al*,1997; Bellasi *et al*, 2006).

Determination of serum calcium level

Calcium level is also predictive factor to determine the vascular calcification which is the risk factor for ischemic heart diseases. A normal serum calcium level is 8-10 mg/dL (2-2.5 mmol/L). Hypercalcemia is defined as a serum calcium level greater than 10.5 mg/dL (>2.5 mmol/L). A high calcium level and phosphorus was determined in patients with ESRD who undergo dialysis (Moe & Chen ,2004).

RESULTS AND DISCUSSION

End stage renal disease (ESRD) is more prevalent in diabetic hypertensive patients and risk of cardiovascular diseases is more in end stage renal disease patients. The treatment of end stage renal disease is only the dialysis and kidney transplant but the cardiovascular death is more prevalent in dialyzed patients due to increased serum phosphate and calcium level in dialyzed patient. Obesity has been identified as a risk factor for single nephron hyperfiltration, increased prevalence of chronic kidney disease (CKD), and higher odds for end-stage renal disease (ESRD). CKD and ESRD in obese individuals develop in an incremental fashion directly proportional to body mass index (BMI), independent of hypertension and diabetes comorbidities. Obese individuals with CKD seem to consume an equivalent amount of daily protein and even fewer total calories compared with obese non-CKD controls; however, their leisure activity is significantly less and they do not pursue weight loss similar to their counterparts. These findings highlight the importance of lifestyle and behavior modification as risks for CKD in obese individuals, although we cannot downplay the role of prevalent comorbidities such as diabetes, hypertension, dyslipidemia, and heart disease in this population. End stage renal disease always comes after chronic kidney disease whose stages are determined by the GFR as given in the Table 1.

Table 1: Estimated values of GFR of renal disease

Stage	description	GFR(mL/min/1.73m^2)
1	Kidne 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(or dialysis)

CONCLUSION

Earlier stages of CKD are defined based on the combination of kidney damage (most often quantified using albuminuria) and decreased kidney function (quantified as glomerular filtration rate [GFR] estimated from the serum creatinine concentration). Estimation of GFR from serum creatinine is the recommended approach for CKD staging at this time and increasing evidence shows a strong association with risk even when applied to the general population. Because individuals with early stages of CKD have a higher risk of cardiovascular disease morbidity and mortality than their risk of progression to kidney failure, cardiovascular risk factor management is critical. The high prevalence of CKD overall, and particularly among older individuals and persons with hypertension and diabetes, suggests that CKD needs to be a central part of future public health planning.

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