Introduction

Chronic Kidney Disease is a gradual loss of Kidney Function. Over a period of Months and years, a greater increase for the prevalence of chronic kidney disease (CKD) in the population has led to improvements in affinity and diagnosis of chronic kidney diseases. The CIMT (Carotid Intima Media Thickness) of common carotid artery is evaluated as an early marker for atherosclerosis. The normal intima - media thickness of common carotid artery is evaluated by B mode ultrasound imaging was 0.74 ±0.14mm.

Methods

In this study, we reviewed various observational articles, clinical and experimental studies and from electronic databases (PUBMED and Cochrane Central Register of Controlled Trials) for potentially relevant articles comparing various studies from January 2010 to December 2018 published in English. Keywords used for search included: Carotid Intima Media Thickness.
Media Thickness, Chronic Kidney Disease, Cerebrovascular disease, Renal function Test

**Epidemiology**

In India>1 billion population are prone for CKD which is likely to pose major problems for both healthcare and the economy in future years. Indeed , it has been estimated that age–adjusted incidence rate of ESRD in India to be 229 per million population. The numbers of CKD cases are on the rise in developing countries mainly in India and China. This rise can be attributed to the increase in life expectancy of people of developing countries. The most common cause for CKD is diabetes and hypertension. In western population about two-third of the CKD population is suffering from diabetes or hypertension or both. In Indian scenario, 40-60 percent of CKD patient are found to be suffering from at least one of the two comorbidities. As India is the diabetic capital of the world and number of hypertensive are also increasing, the estimated individuals suffering from CKD is expected to increase. These individuals with risk factors thus become the key target population to address to reduce the burden of CKD. The common cause of CKD in India is Diabetic Nephropathy. The second most common cause of CKD is chronic glomerulonephritis followed by hypertensive nephrosclerosis. About 48% cases presented in stage 5 and were younger (less than 40 years) than those in Stages III-IV. Diabetic nephropathy patients were older, generally presented in earlier stages of CKD at presentation. When the data of each zone was closely monitored, it was observed that south of India had the maximum cases of CKD with undetermined aetiology (20%) while East zone had least (10%).

**Classification of Ckd**

Classification of CKD are many types for staging of CKD. The commonly used criteria is KDIGO classification was started in 2002. Classification and stratification was done by the American journal of kidney disease. In 2004 KDIGO approached with definition and classification of CKD which was modified in KDIGO 06 CC, KDIGO 09CCand KDIGO CPG on CKD in 2013. The 2013 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease (CKD) provides guidance on management of lipid and treatment for all patients with CKD. The guideline has chapters dealing with assessment of lipid status and treatment for dyslipidaemia in adults and children. The latest guidelines of KDIGO 2017 deals with Mineral bone disorder (MBD).

**Stages of Ckd**

<table>
<thead>
<tr>
<th>Stage Description</th>
<th>GFR(ml/min/1.7m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Kidney damage normal or ↑GFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2. Kidney damage with mildly ↓GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3. Moderate decrease in GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4. Severe decrease in GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5. Kidney failure</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

**Risk Factors of Ckd**

Table 2 Risk factors for Cardiovascular disease in CKD

<table>
<thead>
<tr>
<th>Traditional</th>
<th>Non-traditional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Inflammation</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>Oxidative stress</td>
</tr>
<tr>
<td>Smoking</td>
<td>Hyperhomocysteinaemia</td>
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<tr>
<td>Older Age</td>
<td>Anemia</td>
</tr>
<tr>
<td>Gender</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Higher LDL Cholesterol</td>
<td>calcium/phosphate</td>
</tr>
<tr>
<td>Lower HDL Cholesterol</td>
<td>metabolism</td>
</tr>
<tr>
<td>Family History of CVD</td>
<td>Lipoprotein(a) and apoB/apoA1</td>
</tr>
<tr>
<td>Menopause</td>
<td>Advanced glycation and end products</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>Endothelial dysfunction</td>
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<tr>
<td>LVH</td>
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</tbody>
</table>

**Traditional Factors**

**Family history:** family members of CKD patients have higher prevalence of CKD.

**Gender:** Studies have shown that Chronic kidney disease (CKD) is more common in men.

**AGE :** Renal function decreases with age its common in both men and women.

**Obesity:** One of the strongest risk factors for ESRD in twenty first century is obesity.

**Smoking:** Smoking can increase the risk of CKD through pro-inflammatory state, oxidative stress, pro-thrombotic shift, endothelial dysfunction, glomerulosclerosis and atrophy of the tubules.

**Alcohol:** Alcohol is commonest risk for CKD progression.

**Diabetes mellitus:** Diabetes mellitus (DM) is the common cause of CKD and end stage renal disease (ESRD) in developing countries. Mechanism that lead to kidney disease in diabetes include hyper filtration injury, advanced glycosylation and end products, and reactive oxygen species.

**Hypertension:** Hypertension has been long time risk factor in patients with CKD and ESRD. It accounts for 27% of all ESRD patients and 28% of haemodialysis patients. Systemic hypertension is transmitted to intraglomerular capillary pressure leading to glomerulosclerosis and decrease renal function. The variable risk for impaired renal function is among patient with hypertension.

**Dyslipidaemia:** The most common lipid abnormality in kidney failure is an accumulation of low density lipoprotein(LDL) with elevated serum triglycerides and decreased high density lipoprotein(HDL) cholesterol levels.

**Non -Traditional Factors**

**Inflammation:** Inflammation is common to both CKD and Cardiovascular disease and it is an important role in between two systems. There is a evidence from both clinical and experimental studies that inflammation plays a role in pathogenesis of atherosclerosis.

**Oxidative Stress:** It is defined as tissue injury resulting from an excess of oxidant compounds, which are crucial for tissue repair and protection against infection. Oxidized low density lipoprotein in blood plays a major role in pathogenesis of coronary heart disease, hypertension. It is well established that
CKD patients, most specifically Renal replacement patients have elevated levels of markers of oxidative stress compared with general population.

**Hyperhomocystinaemia:** Chronic kidney disease is closely associated with elevated levels of homocysteine, which has been linked with CVD. A causal relationship may exist between hyperhomocystinaemia and renal impairment; available evidence suggests that elevated homocysteine levels have a strong inverse correlation with GFR; in addition, the levels were reduced after kidney transplantation.

**Clinical Presentation Ckd**

Pathological changes in the cardiovascular system can be broadly divided into those that affect the vessels (specially arteries) and heart structures.

**Arterial Disease:** The term “arteriosclerosis” generally used to describe a range of vascular pathologies derived from Greek word meaning “hardening of vessels”. However, the termStringly refers to atherosclerosis, arteriosclerosis, and Monckerberg’s medial calcific sclerosis. Atherosclerosis is characterized by the development of lipid-enriched plaques in the intima layer of the artery. Occurrence of calcification in plaque is important feature of atherosclerosis. In contrast, arteriosclerosis, which was first described in patients with Bright’s disease in 1868, is characterized by noncalcified, nonatheromatous thickening of smaller muscular arteries. The third distinct form of arterial disease was described in 1903 by mock Enberg. It is characterized by non-atheromatous thickening and heavy calcification involving tunica media of the artery. Chronic kidney disease patients may be affected by all of the three aforementioned forms of arterial disease. Arteriosclerosis in an individual will be determined by various factors including the patient’s age. Exposure to risk factors as well as duration of CKD.

**Cardiac Disease:** Left ventricular remodelling develops well before initiation of dialysis and may even be detectable in patients with CKD stage 2 or 3. Association between CKD and CVD was first observed among young dialysis patients, with increased left ventricular mass reported in 74% of them. Left ventricular hypertrophy(LVH) is commonly categorized according to the predominant pattern of abnormality on echocardiogram. Foley et al. described concentric hypertrophy and eccentric hypertrophy in 44% and 30% of their studied population respectively. Concentric LVH is associated with pressure overload (typically accompanying hypertension, arteriosclerosis or occasionally aortic stenosis) and is characterized by increased wall thickness and normal or decreased left ventricular chamber. Eccentric LVH is characterized by an increase in myocyte length that is proportional to the increase in the left ventricular diameter. Risk factors for eccentric LVH include volume overload secondary to salt and water retention, anaemia and arteriovenous fistula.

**Left ventricular Hypertrophy:** Stewart et al. in their study of 298 patients with CKD demonstrated LVH in all stages of CKD, progressing with deteriorating renal function. Similarly, in an earlier report by Levin et al. prevalence of LVH increases with advancing CKD. Left ventricular hypertrophy was found in 27.6% of patients with creatinine clearance (CrCl) greater than 50ml/min, 30.8% of those with CrCl between 25 and 49ml/min, and 45.2% of patients with CrCl of <25ml/min. In addition, the mean left ventricular mass index in patients with CrCl greater than 50ml/min, 25-50 ml/min and less than 25ml/min were 97.5 g/m2. In CKD patients, uraemia facilitate abnormal structural remodelling of the heart, resulting in LVH, fibrosis and left ventricular dysfunction. This together with electrolyte abnormalities may trigger and facilitates arrhythmias which is commonly seen in ESRD patients.

**Pericardial Disease:** Uremic pericarditis is a complication of end stage of CKD. It is an absolute indication for initiating dialysis.

**Neurovascular Abnormalities:** Stroke is the third leading cause of cerebrovascular accident death among persons with end-stage kidney disease (ESKD) on dialysis. Increased chronic inflammation and oxidative stress, decreased nitric oxide production, and hyperhomocystinaemia that might induce endothelium dysfunction, platelet aggregation, and vascular injury contribute to neurological insults in CKD patients.

**Anemia:** Normocytic normochromic anaemia is common in CKD. The causes for anaemia in CKD are relative erythropoietin deficiency, reduced RBC life span, bleeding diathesis, iron deficiency, hyperparathyroidism/ bone marrow fibrosis, chronic inflammation, folate or vitamin b 12 deficiency, haemoglobinopathy. The recommendation that patients with CKD be periodically evaluated for anaemia rests on observations that, in the absence of use of erythropoiesis-stimulating agents, (ESAs), there is often a gradual decline in HB over time in patients with CKD as the level of GFR declines suggesting the need for regular surveillance of Haemoglobin concentration.

**Abnormal Haemostasis:** Late stages of CKD presents with prolongation of bleeding time, decreased activity of platelet factor III, abnormal platelet aggregation and adhesiveness. This may lead to bruising and bleeding, menorrhagia and GI bleed.

**Atherosclerosis in Chronic Kidney Disease:** Atherosclerosis is a frequent cause of morbidity in patients with end-stage renal disease. The high prevalence of cardiovascular mortality in chronic haemodialysis patients reported in early reports has been extensively confirmed by numerous subsequent studies. Atherosclerosis is advanced in renal failure, i.e. atherosclerotic lesions develop early on in the course of renal dysfunction and show increased size, and there are indeed some specific morphological findings in arteriosclerosis, i.e. thickening of the vascular wall of peripheral arteries, and atherosclerosis, i.e. plaque formation elastic type arteries, under the condition of renal failure. Hypertriglyceridemia is an early feature of CKD. It persists at every stage of renal dysfunction, and is found in the majority of patients with ESRD, particularly diabetics and those undergoing peritoneal dialysis. Hypertriglyceridemia reflects increased synthesis by the liver and especially decreased clearance because of decreased activity of lipoprotein enzymes, including lipoprotein lipase and hepatic lipase, and reduction in their inhibitors, such as preβ HDL, reduced apolipoprotein CII and apoE.
Markers of Vascular Disease

lipids

Carotid Artery Intima Media Thickness

Carotid artery intima-media thickness (CAIMT) is increasingly used as a surrogate marker of early atherosclerosis, and in a recent review it was shown that CAIMT is a strong predictor of future vascular events such as myocardial infarction and stroke. The normal intima – medial thickness of common carotid is evaluated by B-mode ultrasound imaging. The normal reference value 0.74±0.14mm. Some studies also indicated that CAIMT <0.8 mm is associated with normal healthy individuals, and a value of CAIMT at or above 1mm is associated with atherosclerosis and a significantly increased cardiovascular disease (CVD) risk in any age group. Kumar et al. and Howard et al. observed that CAIMT of healthy controls were 0.73mm and <0.7 mm, respectively. In a study they found that serum phosphate level was a significant independent risk factor for increased carotid intima media thickness in haemodialysis patients.

Many epidemiological studies have displayed an association between CAIMT and the risk of coronary artery disease. CAIMT has been used as a research tool in epidemiological and clinical trials. Over the last few years, measurement of the layers of the arterial wall and plaques has been made possible in large population samples due to advancement in non-invasive ultrasound skills. CAIMT measurement is relatively safe and inexpensive. As there is no radiation involved, contrast is not needed. Lumen diameter does not affect ultra sonographic measurement of the IMT, it may therefore, be considered as the most precise method of assessing early development of atherosclerosis in large population samples.

Carotid intima-media thickness (CIMT) is a non-invasive marker that suggests the presence of generalized atherosclerosis and is also a good indicator of the presence of coronary artery disease. In the Kuopio Ischemic Heart Disease risk factor study, every 0.01 cm increment in CAIMT was associated with an 11 percent increased possibility of heart disease.

It has been projected that CAIMT may provide a direct measure of the amount of atherosclerosis present, thus improving cardiovascular risk stratification. In a systematic review and meta-analysis, adding a one time measurement. The Framingham Risk Score was related with a small improvement in 10 year risk prediction of first time heart attack or stroke, but the authors concluded that it is not likely to be clinical importance. Serial measurements of the CAIMT may be more predictive of risk than a one-time measurement. However, one meta-analysis of available studies did not show CAIMT progression, as assessed by serial measurements, to be related to increased risk of cardiovascular events.

Cardiac CT and Calcium Scoring: CAC scoring is an inexpensive technique to determine the definite presence and degree of calcified coronary artery plaques. No intravenous access is needed, and patients do not require any special preparation apart from practising how to hold their breath and remain still during the examination. The use of beta blockers is optional and may have a small benefit in patients who have an elevated heart rate. Scans should be acquired using an axial mode with prospective electrocardiogram triggering during diastole. The scan settings include a tube voltage of 120 kV, while the tube current should be altered according to patient size in order to achieve adequate balance between radiation dose and image noise. The amount of calcium is measured using the Agatston score, which is based on multiplying each area of calcified plaque by the corresponding CT density.

Coronary CT Angiography: It is a non-invasive angiography and plaque is also visualized. But radiation exposure is hazard before PTCA for CABG. Coronary CTA requires the administration of intravenous contrast to visualize non-calcified plaque and estimate the severity of luminal stenosis. It allows for high-resolution assessment of the presence, extent and severity of coronary plaque.

Before performing a coronary CTA, contraindications, such as known iodine contrast allergy, inability to follow breath-hold instructions, pregnancy and renal insufficiency, should be reviewed. Moreover, probable patient-related technical issues that may interfere with the image quality, such as obesity and active cardiac arrhythmias, should be reviewed. To improve image quality, a slow and regular heart rate is preferred, usually, 60 beats per minute. For individuals with faster heart rates, beta blockers can be prescribed. Nitrites may also be used to dilate the coronary arteries and improve image quality.

Method for Assessment of Plaque Morphology

Intravascular Ultrasound (IVUS) and OCT: These are invasive and catheters are costlier than simple catheters. But these give view of atheroma. Optical coherence tomography (OCT) gives magnified and detail visualization of plaque and its morphology.

By PET- imaging. one can also visualize status of plaque morphology and composition. But, not only there is exposure to radiation, it is costly also and it is available in tertiary centres. As of now, it is mainly used for research.

CONCLUSION

CKD is the independent risk factor for CVD and majority of patients expire due to CVA and CVD than progress to ESRD. CKD further increases the risk of cerebrovascular accidents in patients with vascular risk factors. Carotid Intima Media Thickness, Cardiac CT calcium scoring, Coronary CT angiography, Intravascular ultrasound, Optical coherence tomography PET – imaging is a non-invasive marker of vascular accidents in patients with CKD.

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References


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