ASSESSMENT AND PREVENTION OF RISK FOR DEVELOPMENT OF CARDIOVASCULAR DISEASES IN GERIATRIC POPULATION WITH CHRONIC KIDNEY DISEASE

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CONTENTS

LIST OF ABBREVATIONS

ACE	-	Angiotensin converting enzyme
ADH	-	Antidiuretic hormone
ARF	-	Acute renal failure
ACE-I	-	Angiotensin-converting Enzyme Inhibitor
ARB	-	Angiotensin Receptor Blocker
AMI	-	Acute Myocardial Infraction
BP	-	Blood Pressure
CK	-	Creatinine kinase
CKD	-	Chronic kidney diease
CKMB	-	Creatinine kinase myocardial bound
Clcr	-	Creatinine clearance
CRF	-	Chronic renal failure
CT	-	Computed tomography
CVR	-	Cardiovascular risk
DM	-	Diabetes mellitus
DHCCB	-	Dihydropyridine Calcium Channel Blocker
eGFR	-	Estimate of glomerular filtration rate
ESRD	-	End Stage Renal Disease
GFR	-	Glomerular filteration rate
GBD	-	Global Burden of Disease
GDT	-	Global Differentiation Factor
HDL	-	High-Density Lipoprotein
HOT	-	Hypertension Optimal Treatment

IVU	-	Intravenous urography
KDOQI	-	Kidney disease quality outcome initiative
LDL	-	Low-density Lipoprotein
MCP-1	-	Monocyte chemoattractant protein
MDRD	-	Modification of diet in renal disease study
MRA	-	Magnetic Resonace angiography
MRI	-	Magnetic resonace imaging
MOZART	-	Magnetic Resonance Imaging and Elastography in Ezetimibe
Na	-	Sodium
NDH-CCB	-	Nondihydropyridine Calcium Channel Blocker
NSAIDs	-	Nonsteroidal Anti-inflammatory Drugs
NASH	-	Nonalcoholic Steatohepatitis
RAAS	-	Renin angiotensin-aldosterone system
RANTES	-	Regulated upon activation normal T-cell expressed and secreted
RRT	-	Renal replacement therapy
SHT	-	Systemic hypertension
Seq	-	Sequestrants
TG	-	Triglycerides
TLC	-	Therapeutic Lifestyle Changes
WHO	-	World health organization

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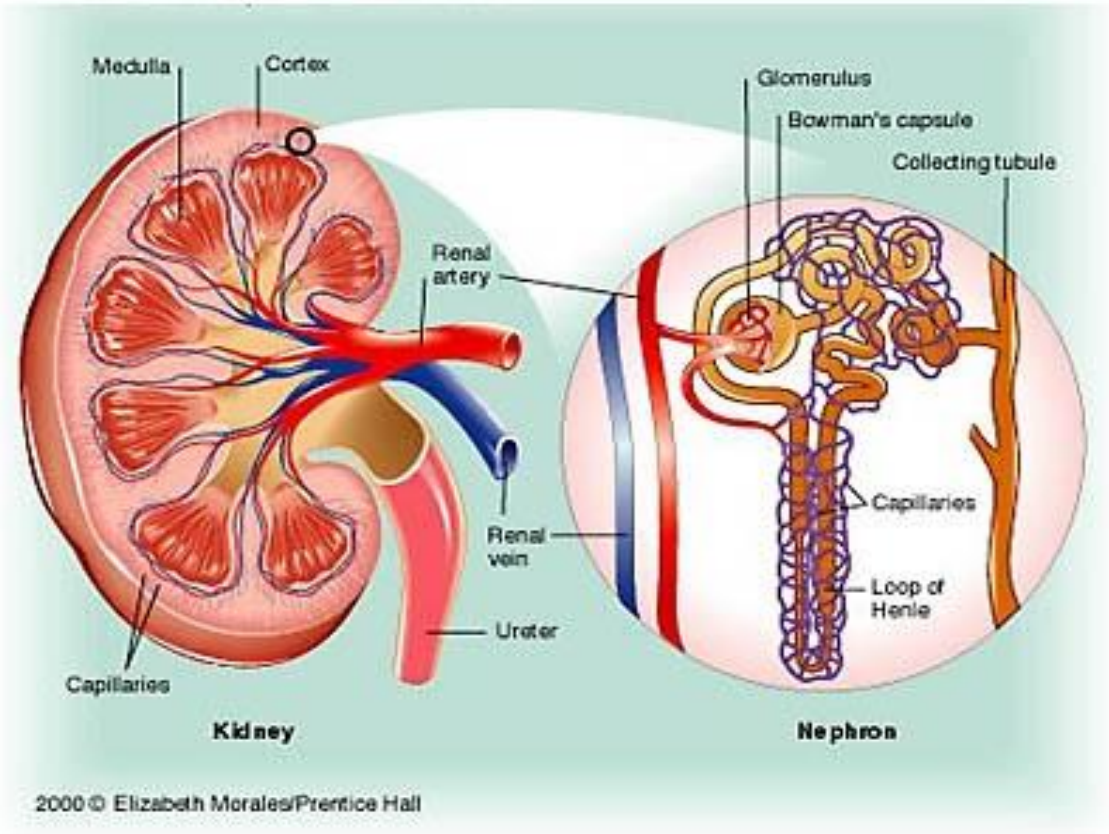
ABSTRACT

Chronic kidney disease is a large and growing problem among aging populations. The studies shows that the patients with chronic kidney disease are at increased risk of cardiovascular events even at early stage of kidney disease.Men are at increased risk of getting cardiovascular disease than women. The study was carried out to assess and prevent the cardiovascular risk in geriatric patients with chronic kidney disease getting admitted to the study site. Study populations of 102 geriatric patients were included as per the inclusion criteria and data were collected in a specially designed data entry format. The collected data were screened to identify the cardiovascular risk in geriatric patients by using WHO risk scale, Framingham's risk calculator and QRISK calculator. From the study it was found that diabetes mellitus and hypertension were the major problems may pose risk for cardiovascular disease in geriatrics. The present study had a various drugs prescribed for the study population including anti-hypertensives, anti-coagulants, anti-diabetics and proton pump inhibitors and diuretics. This study also revealed the importance of prevention of cardiovascular disease. The reasons for admission for the study population was found to be difficulty in breathing, vomiting, decreased urine output, chest pain, etc. Route of administration for drug administered to the study population was analyzed and there was at least one drug administered as an injection to 83.33% patients. Length of stay for the study population in hospital was calculated and found that a minimum of 2 days and maximum of 15 days. Analysis of drug – drug interaction's prevalence in the study population revealed that 57% of the prescriptions do not have any such interactions. The core analysis of this work is assessment of CV risks in the geriatric study population with chronic kidney disease using three various scale that had revealed that 40% of the study population was in very high risk category and 20 & 32% were in high and moderate risk category respectively. The study population were counseled and intervened appropriately about various risks and its management to prevent themselves from entering into the next higher risk category.

1.INTRODUCTION

Anatomy and Physiology of Kidney[1]

Fig.No.1:-Anatomy of kidney[1]



Every day the kidneys filter nearly 200 liters of fluid from the bloodstream, allowing toxins, metabolic wastes, and excess ions to leave the body in urine while returning needed substances to the blood. The bean-shaped kidneys lie in a retroperitoneal position (between the dorsal body wall and the parietal peritoneum) in the superior lumbar region. A frontal section through a kidney reveals three distinct regions :cortex, medulla, and pelvis. **Nephrons** are the structural and functional units of the kidneys. Each kidney contains over 1 million of these tiny blood-processing units, which carry out the processes that form urine. In addition, there are thousands of collecting ducts, each of which collects fluid from several nephrons and conveys it to the renal pelvis. Each nephron consists of a **glomerulus**, which is a tuft of

capillaries, and a **renal tubule**. The renal tubule has a cup-shaped end, the **glomerular capsule**(or **Bowman's capsule**), which is blind and completely surrounds the glomerulus. Collectively, the glomerular capsule and the enclosed glomerulus are called the **renal corpuscle**[1]. The detailed diagram is shown in **Fig.no.1**.

Kidney Diseases

Kidney diseases are classified into two:Acute kidney disease and chronic kidney disease.Acute renal failure (ARF) is a common and serious problem in clinical medicine. It is characterised by an abrupt reduction (usually within a 48-h period) in kidney function[2]. It is also a condition in which a previously normal serum creatinine rises by 0.5 mg/dL, or an absolute increase in serum creatinine of >1 mg/dL in a patient[3].

Chronic kidney disease (CKD) is a reduction in the glomerular filtration rate (GFR) and/or urinary abnormalities or structural abnormalities of the renal tract2.The name chronic kidney disease was proposed by the National Kidney Foundation–Kidney Disease Quality Outcome Initiative (K/DOQI) as a way of simplifying and codifying the language used to communicate about the disease. CKD is also defined as either of the following conditions i.e for a minimum of 3 months: glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2, or damage to the kidney(s) with or without a decrease in GFR. This damage may be evidenced by abnormalities in the composition of blood or urine, or by changes seen in imaging studies. The K/DOQI Working Group further categorizes the extent of kidney disease according to the presence of kidney damage and the GFR. Stage I CKD is defined as the presence of kidney damage even though GFR may be normal or elevated as ≥90 mL/min/1.73 m2. Stage II CKD is evidenced by a GFR between 60 and 89 mL/min/1.73 m2. Patients with Stage III CKD may or may not have kidney damage, while their GFR is reduced to between 30 and 59 mL/min/1.73 m2. CKD patients with Stage IV disease also may not have intrinsic kidney damage, but their GFR is severely reduced to between 15 and 29 mL/min/1.73 m2. The last stage, Stage V, is also known as end-stage kidney disease (ESKD). This condition, formerly known as end-stage renal disease (ESRD) which is defined as a GFR less than 15 mL/min/1.73 m^2 or the need for renal replacement therapy (RRT) for survival. The **Tab.No.1** will give a detailed description of CKD.

Most forms of kidney disease will cause irreversible, progressive deterioration of kidney function if not identified and treated properly. Depending on the cause, the disease may progress to complete loss of function over months to years. As the extent of deterioration increases, the kidney is unable to perform normal homeostatic functions. This leads to fluid and electrolyte abnormalities, acid-base disturbances, hormonal dysregulation, and other systemic disturbances. When the GFR falls to below 15 mL/min/1.73 m2, patients generally require some form of RRT for survival. Options for RRT include hemodialysis, peritoneal dialysis, and kidney transplantation. Although patients may be maintained on dialysis or may receive a kidney transplant but they have increased risks of morbidity and mortality[4].

Tab.No.1:-Classification of Chronic Kidney disease[4]

Classification	Damage	GFR (ml/min.)
Increased risk of kidney disease	Risk factors for CKD(diabetes,HTN,family history of CKD)	≥90
Stage 1	Kidney damage with normal GFR	≥90
Stage II	Kidney damage with mild decrease in GFR	60-89
Stage III	Moderate decrease in GFR	30-59
Stage IV	Severe decrease in GFR	15-29
Stage V	Kidney failure	<15
CKD-chronic kidney disease; GFR-glomerular filtration rate; HTN-hypertension		

Renin-angiotensin-aldosterone system[2]

The renin-angiotensin-aldosterone system (RAAS) has a critical role in the progression of CKD and an awareness of this system is important for understanding the pathophysiology of CKD and the targets for therapeutic intervention. Most of the renal effects of this system are through regulating intraglomerular pressures, salt and water balance. Renin is an enzyme which is formed and stored in the juxtaglomerular apparatus and released in response to decreased afferent intra-arterial pressures, decreased glomerular ultrafiltrate sodium levels and sympathetic nervous system activation. In patients with CKD,

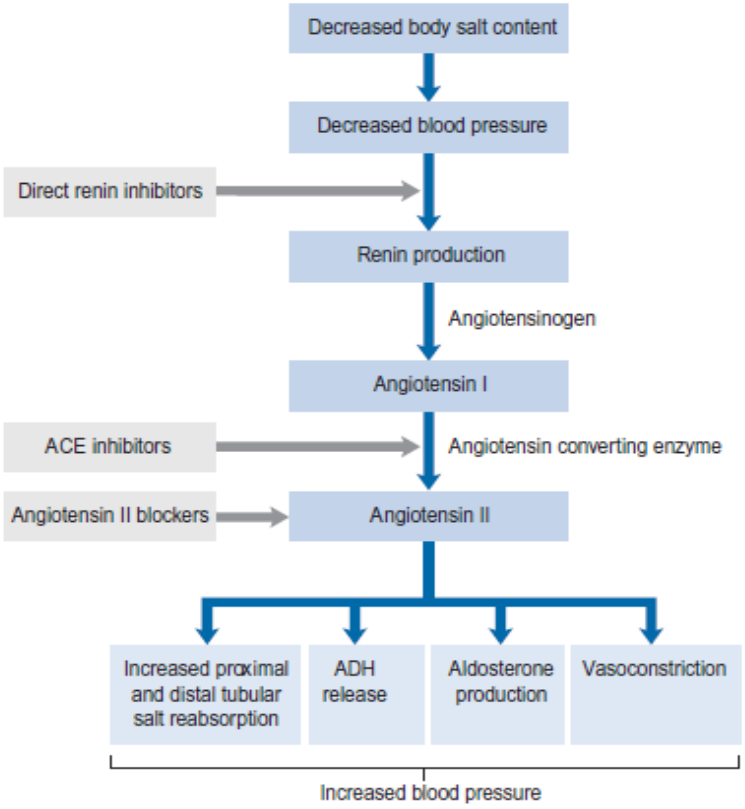
intra-renal pressures are often low and sympathetic over activity is common; these factors lead to increased renin secretion. This can occur with normal or elevated systemic blood pressure.Renin promotes cleavage of the protein angiotensinogen, which is produced by the liver, to produce angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE). Angiotensin II has two major physiological effects. First, it acts on the zona glomerulosa ofthe adrenal cortex to promote production of the mineralocorticoid hormone aldosterone, with resultant increased distal tubular salt and water reabsorption. Furthermore, it promotes antidiuretic hormone (ADH) release, which increases proximal tubular sodium reabsorption and promotes thirst. In combination, these lead to salt and fluid retention, high intravascular volumes, hypertension and oedema. Second, it is a direct vasoconstrictor and promotes systemic and (preferential) renal hypertension. The renal effects are predominantly on the efferent glomerular arteriole. Vasoconstriction at this site is mediated by a high density of angiotensin II receptors. When these receptors are ligated by angiotensin II, there is increased intra- glomerular pressures. Whilst this leads to an overall increase in GFR in the short-term, over a longer period glomerular hypertension promotes accelerated glomerular scarring and worsening CKD. In addition to the vascular and endocrine effects of the RAAS, it is now recognised that there is a local immune modulatory role for this system. Both resident (e.g. tubular epithelial) cells and inflammatory (monocytes and macrophages) cells synthesis components of the RAAS and are themselves targeted by the system. The RAAS is depicted in the following **Fig.No.2**

Causes of CKD[2]

The reduction in renal function observed in CKD results from damage to the infrastructure of the kidney in discrete areas. The nephron is the functional unit of the kidney, as nephrons become damaged and fail, remaining nephrons compensate for loss of function by hyperfiltration secondary to raised intra-glomerular pressure. This causes damage with secondary nephron loss. The patient remains well until so many nephrons are lost that the GFR can no longer be maintained despite the activation of compensatory mechanisms. As a consequence there is a progressive decline in kidney function.CKD arises from a variety of causes which are listed in **Tab.No.2** are ordered according to prevalence. It is important to note the prevalence of these factors are different in CKD and end stage renal disease.CKD arises from a variety of causes such as Glomerulonephritis, Pyelonephritis, Diabetes,

Polycystic kidney and hypertension. Renal vascular disease although by the time a patient has established CKD it may not be possible to identify the exact cause.

Fig.No.2:-Renin angiotensin –aldosterone system[2]



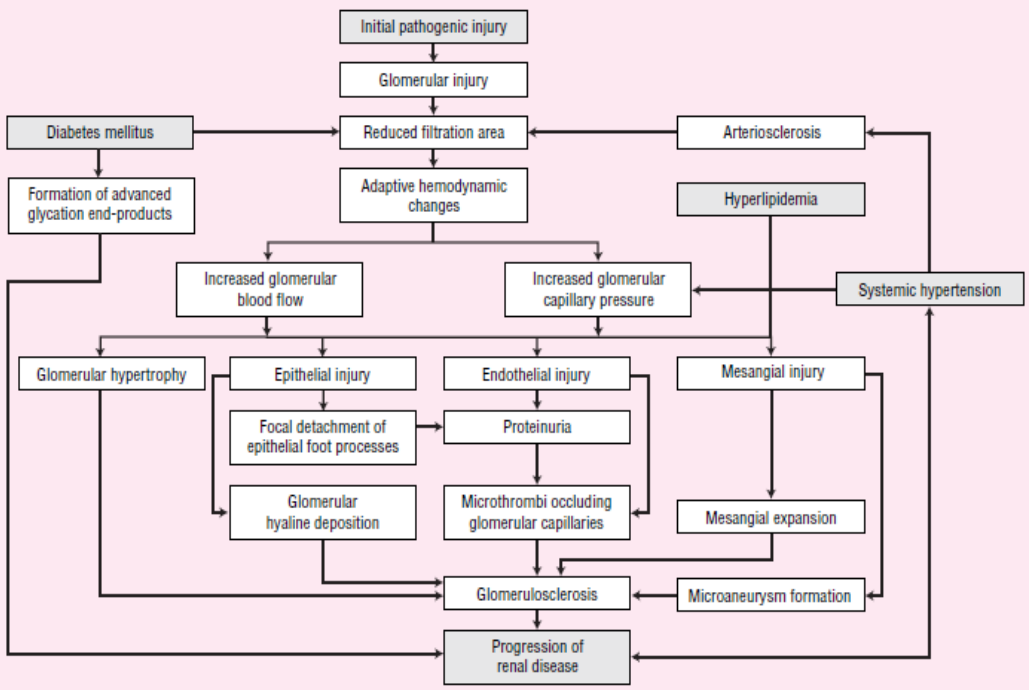
Tab.No.2: – Causes of CKD[2]

Primary diagnosis	Overall%
Uncertain aetiology	21.6
Glomerularnephritis	15.3
Pyelonephritis	11.9
Diabetes	13.4
Polycystic kidney	9.2
Hypertension	5.4
Renal vascular disease	3.2

Pathophysiology[3]

The presence of or exposure to the initiation risk factors results in loss of nephron mass. The remaining nephrons compensate for the loss of renal function and nephron mass. Initially this compensatory hypertrophy may be adaptive. Yet over time the hypertrophy often becomes maladaptive and leads to the development of glomerular hypertension, possibly mediated by angiotensin II which is a potent vasoconstrictor of both the afferent and efferent arterioles, preferentially affects the efferent arterioles, leading to increased pressure within the glomerular capillaries. The development of intraglomerular hypertension generally correlates with the development of systemic arterial hypertension. The resultant proteinuria is thought to accelerate the progressive loss of nephrons due to direct cellular damage. The filtered proteins consist of albumin, transferrin, complement factors, immunoglobulin, cytokines, and angiotensin II, which have varying molecular weights. The pathophysiology is shown in **Fig.No.3** as a schematic representation. Numerous studies have demonstrated that the presence of these proteins in the renal tubule activate tubular cells which leads to the unregulated production of inflammatory and vasoactive cytokines, such as endothelin, monocyte chemoattractant protein (MCP-1), and RANTES (regulated upon activation, normal T-cell expressed and secreted)

Fig.No.3:- Pathophysiology of chronic kidney disease.[3]



Measurement of renal function[2]

The GFR is defined as the volume of filtrate produced by the glomeruli of both kidneys every minute and is a reliable indicator of renal function. It is expensive to measure GFR by gold standard tests such as inulin or radiolabelled isotope clearance. These tests are only used when extremely accurate assessment of kidney function is required. There are equations which can provide an estimate of glomerular filtration rate (eGFR) based on the combination of serum or plasma creatinine. The commonest eGFR equation used in clinical practice is the four-variable MDRD (Modification of Diet in Renal Disease Study) equation. The biochemical variable that provides the basis of the MDRD and most other GFR equations is serum creatinine.

Serum creatinine: Measurement of serum creatinine can be utilised to give an estimate of the kidney function. It is important to note, however, that creatinine also undergoes significant tubular secretion (~10–20%). This becomes important in advanced CKD (stages 4 and 5) and limits the value of measuring serum creatinine to determine renal function in advanced CKD.

MDRD glomerular filtration rate equation: The MDRD equation is more accurate than serum creatinine alone as an estimator of kidney function; those with creatinine levels within the normal range or transplant recipients. The CKD classification system is based on the MDRD eGFR.

eGFR (mL/min/1.73m2) = 186 x [serum creatinine (μmol/L)/88.4]–1.154 x [age]–0.203 x [0.742 if **female**] x [1.212 if **African-American**]

Cockroft–Gault equation: The Cockroft–Gault equation uses weight, sex and age to estimate creatinine clearance and was derived using average population data.

$$CIcr = \frac{F\ (140 - \text{age (years)}) \times \text{weight (kg)}}{\text{Serum creatinine (}\lceil\text{mol/L)}}$$

where ***F*** = 1.04 (females) or 1.23 (males)

Creatinine clearance: It is a measurement of the volume of blood that is cleared of creatinine with time. Measurements of creatinine clearance (ClCr) require accurate collection of 24 h urine samples with a serum creatinine sample midway through this period.

$$ClCr = \frac{U \times V}{S}$$

where ***U*** is the urine creatinine concentration (μmol/L), ***V*** is the urine flow rate (mL/min) and ***S*** is the serum creatinine concentration

Clinical Presentation of Chronic Kidney Disease[3]

CKD development and progression is typically insidious in onset, often with the absence of any noticeable symptoms. At a minimum, the diagnosis of CKD requires measurement of serum creatinine, calculation of GFR and assessment of a urinalysis for urinary microalbumin or total protein. The diagnosis of Stages 3, 4, and 5 CKD requires the work-up for other common complications including anemia, cardiovascular risks, metabolic bone disease, malnutrition, and disorders of fluids and electrolytes.

SIGNS AND SYMPTOMS

Symptoms are generally absent in CKD Stages 1 and 2, and may be minimal during Stages 3 and 4. Classic symptoms associated with Stage 5 CKD include pruritus, dysgeusia, nausea, vomiting and bleeding abnormalities. Symptoms associated with anemia include cold intolerance, shortness of breath, and fatigue. The severity of symptoms are related to the rate of anemia development and the degree of haemoglobin reduction.The following signs shall be observed during CKD.

Cardiovascular: Leftventricular hypertrophy, congestive heart failure, hyperhomocysteinemia, dyslipidemia, palpitations, arrhythmias, electrocardiographic changes, elevated creatinekinase-myocardial bound (CK-MB) and creatine kinase (CK), worsening hypertension, and oedema.

Musculoskeletal: Cramp and muscle pain.

Neuropsychiatric: Depression, anxiety, impaired mental cognition, fatigue, and sexual dysfunction.

Gastrointestinal: Gastroesophageal reflux disease, constipation,GI bleeding, nausea, and vomiting.

Laboratory Investigations

Structural assessments of the kidney may be performed using a number of imaging procedures, including ultrasonography, intravenous urography (IVU), plain abdominal radiography, computed tomography (CT), magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA).

Treatment[1]

The overall aims of the treatment of CKD can be summarized as follows:

- Reverse or arrest the process causing the renal damage (this may not be possible)
- Avoid conditions that might worsen renal failure
- Treat the secondary complications of CKD (renal anaemia and bone disease)
- Relieve symptoms
- Implement regular dialysis treatment and/or transplantation at the most appropriate time.

Treatment of Diabetic Nephropathy

Diabetic nephropathy is caused mainly by the presence of hyperglycemia, as previously discussed. In this situation, the best way to prevent or slow renal damage is to prevent hyperglycemia.

Treatment of Hypertension with Antihypertensive Agents

The following treatment strategies are used: decrease blood pressure to less than 130/80 mm Hg, reduce proteinuria, slow progression of kidney disease and reduce CVD risk. Some of antihypertensive drugs used for the treatment of CRF is given in following **Tab.No.3**.

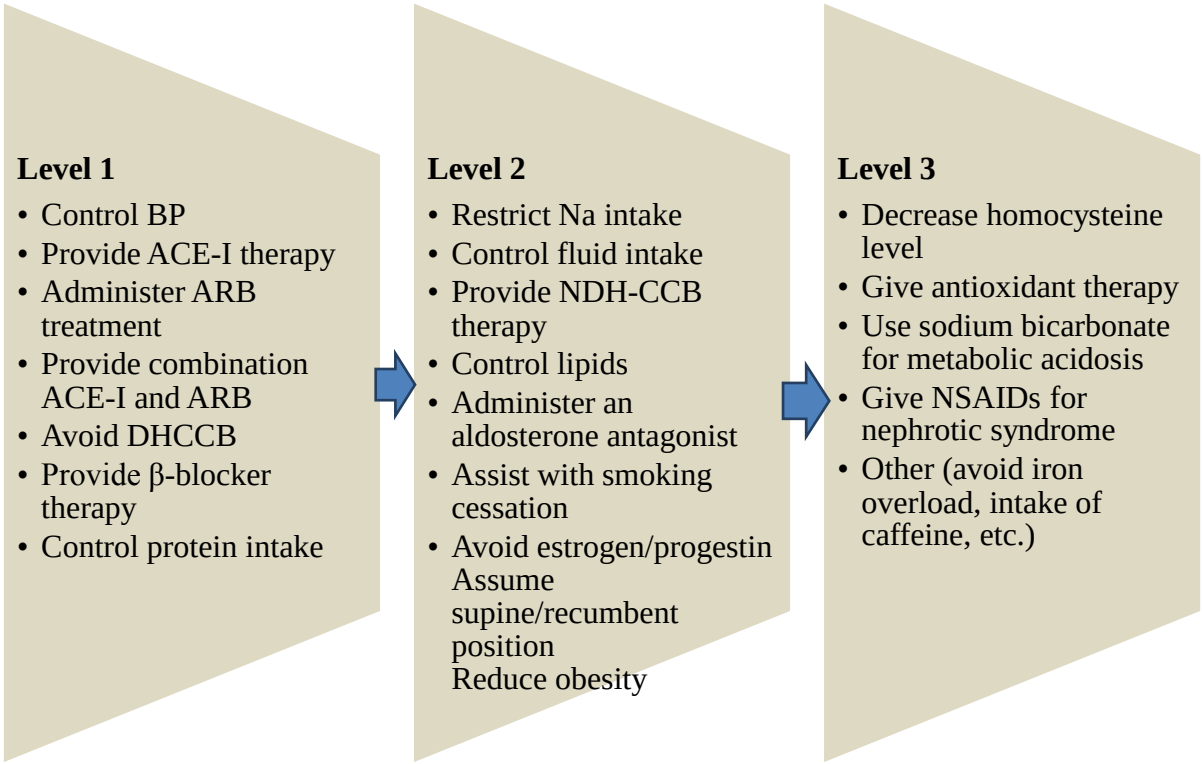
Tab.No.3:- Treatment of hypertension[3]

Effects of antihypertensive agents on renal blood flow(RBF) and glomerular filtration rate(GFR)		
Antihypertensive agent	**Mechanism of action**	**Effects on renal hemodynamic**
Diuretics	Sodium and volume depletion	Decrease in GFR and RBF
	Increase vasodilatory prostaglandin levels	Increase in RBF
	Renal vasoconstriction	Decrease in GFR and RBF
B-adrenergic blockers	Decrease cardiac output	Decrease in GFR and RBF
	Increase renal vascular resistance (nonselective agents)	Decrease in GFR and RBF
	Decrease vascular resistance (β-selective agents)	No change in GFR and RBF
Centrally acting antiadrenergic drugs	Decrease renal vascular resistance	No change in GFR and RBF
	↓ Renal perfusion pressure (clonidine, α2-adrenergic agonist) Decrease in GFR and RBF	↓ Renal perfusion pressure (clonidine, α2-adrenergic agonist) Decrease in GFR and RBF
Peripherally acting antiadrenergic	Peripherally acting antiadrenergic	Peripherally acting antiadrenergic
Direct vasodilator agents	↓ Renal vascular resistance (hydralazine, minoxidil) Increase in RBF and no effect on GFR	Direct vasodilator agents ↓ Renal vascular resistance (hydralazine, minoxidil) Increase in RBF and no effect on GFR
	Arterial vasodilation plus dilatation of venous capacitance	Arterial vasodilation plus dilatation of venous capacitance
Angiotensin-converting enzyme	Angiotensin-converting enzyme	Angiotensin-converting enzyme
Calcium channel blockers ↓ Renal vascular resistance by vasodilation of afferent	↓ Renal vascular resistance by vasodilation of afferent	↓ Renal vascular resistance by vasodilation of afferent

Treatment of Proteinuria[4]

Lowering the total daily protein excretion in the urine and the use of different agents were used to achieve this goal. As previously mentioned, protein is the specific target for treatment. Several strategies have been tried to decrease proteinuria and therefore decrease the rate of decline to ESRD, as well as to reduce morbidity and mortality. The treatment algorithm for protein urea is depicted in the following **Fig.No.4.**

Fig.No.4:-Treatment of proteinuria[4]



ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; DHCCB, dihydropyridine calcium channel blocker; Na, sodium; NDH-CCB, nondihydropyridine calcium channel blocker; NSAIDs, nonsteroidal anti-inflammatory drugs.

Treatment of Dyslipidemia

The benefits of treating dyslipidemia in patients with CKD have been demonstrated through many studies. Specifically, studies suggest that hydroxymethylglutaryl coenzyme A reductase inhibitors (HMG-CoA, statins) are particularly beneficial. Statins may decrease proliferation of mesangialand proximal tubular cells, reducing glomerulosclerosis. The treatment guidelines of dyslipidemia is given below **Tab.No.4**

Tab.No.4:- Treatment Guidelines for Dyslipidemias of CKD[4]

Dyslipidemia	Goal	Initiate	Increase	Alternative
TG ≥500 mg/dL	<500	TLC	Fibrate or niacin	Fibrate or niacin
LDL 100–129	<100	TLC	Low-dose statin	Bile acid seq or niacin
LDL ≥130	<100	TLC + low-dose statin	Max-dose statin	Bile acid seq or niacin
TG ≥200 and non-HDL ≥130	Non-HDL <130	TLC < low-dose statin	Max-dose statin	Fibrate or niacin
CKD, chronic kidney disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein; seq, sequestrants; TG, triglycerides; TLC, therapeutic lifestyle changes.				

Consequences Of CKD[2]

CKD is significant as it indicates the possibility of progression to end-stage renal disease, and a strong association with accelerated cardiovascular disease. The cardiovascular risk increases with the severity of CKD but is detectable at all levels. Thus, it is important to pay particular attention to cardiovascular risk factors such as smoking, cholesterol and blood pressure in patients with CKD. However, it is known from previous studies that these risk factors only contribute around 50% of the total cardiovascular disease risk. It is important to make a distinction between cardiovascular disease related to macrovascular atherosclerosis and that related to microvascular changes, often found in individuals with CKD. The cardiovascular disease found in CKD is more likely to be related to small vessel disease initiated by endothelial dysfunction rather than atherosclerotic disease. In addition, patients with CKD often have associated left ventricular hypertrophy which may be related to chronic

volume overload and uraemia. Progression to more advanced stages of CKD may occur, particularly if the blood pressure is inadequately controlled and there is significant proteinuria, but this is by no means the rule and many patients with CKD remain stable for years or even decades. These patients need to be followed up with regular blood and urine tests to detect progression, if it occurs. Low risk patients, that is, those with unchanging GFR over time, with controlled blood pressure and no proteinuria may not require long-term follow up by a kidney specialist and surveillance can be carried out satisfactorily in primary care. Patients with CKD 1–3 are frequently asymptomatic. The reduction of GFR is insufficient to cause uraemic symptoms and any minor abnormalities in the urine such as proteinuria or haematuria are usually not noticed by patients. There is a frequent association with high blood pressure which may be the cause or a consequence of renal damage.Patients with CKD stages 4 and 5 should usually be followed up in a nephrology clinic because they will require specialist management of the complications of CKD such as anaemia and bone disease, whilst many will also be undergoing preparation for renal replacement therapy.

Cardiovasular Risk

Cardiovascular disease (CVD) is responsible for the majority of deaths in chronic renal failure (CRF).The report showed that there was a high prevalence of CVD in CKD and that mortality due to CVD was 10 to 30 times higher in dialysis patients than in the general population[5]. There is a direct relationship between the degree of kidney dysfunction and cardiovascular risk (CVR). The presence of proteinuria or microalbuminuria is a strong CVR, while the main causes of kidney diseases are diabetic nephropathy and hypertensive nephrosclerosis, accelerated by smoking and dyslipidemia. Thus, increased CVR among patients with CKD is secondary to the accumulation of these risk factors. CVR factors include: hypertension, dyslipidemia, presence of left ventricular hypertrophy,obesity, diabetes mellitus (DM) and some lifestyle- related habits (high-calorie diet, saturated fats, high cholesterol, salt, alcohol consumption, smoking and sedentariness).In addition tothese, there are non-traditional CVR factors, such as inflammation, oxidative stress, persistentinfection, proteinuria and hyperphosphatemia.[2]

1. **Hypertension**: Hypertension results in atherosclerosis which can cause occlusive renovascular disease and small vessel damage. In patients with significant large vessel occlusive disease arteriolar nephrosclerosis, interstial fibrosis and glomerular collapse may be present. These diagnoses account for around 30% of CKD and a smaller

proportion of end stage renal disease. The effective management of hypertension is crucial to reduce renal damage.

2. **Diabetes**: Diabetes mellitus is the most common metabolic disease that leads to CKD, whilst the predominant lesion in glomerular and referred to as diabetic nephropathy. Diabetes accounts for around 13% of CKD and is associated with faster renal deterioration than other pathologies: these patients are at very significant cardiovascular risk by virtue of both CKD and diabetes. Patients with diabetes may present with no proteinuria, micro albuminuria or overt proteinuria, though as the level of proteinuria increases the GFR usually declines and in many patients this represents an inexorable decline towards end stage renal disease.
3. **Chronic glomerularnephritis**: All types of chronic glomerulonephritis (GN) combined cause about 15% of cases of advanced CKD. The commonest cause of glomerulonephritis is IgA nephropathy which is characterised by deposition of polymeric IgA in the glomerulus with subsequent immune activation. Other patterns of glomerulonephritis include membranous nephropathy, where there is granular deposition of immunoglobulin on the glomerular capillary basement membrane. Systemic autoimmune diseases such as systemic lupus erythematosus can cause a variety of types of glomerulonephritis.

The incidence of drug-induced nephrotoxicity has been increasing with the ever increasing number of drugs and with easy availability of over-the-counter medication viz. nonsteroidal anti-inflammatory drugs (NSAIDs),Antibiotics, angiotensin converting enzyme inhibitors (ACEI) and contrast agents are the major culprit drugs contributory to kidney damage. Drug-induced acute renal failure (ARF) accounted for 20% of all ARF in an Indian study; of which aminoglycosides accounted for 40% of total cases[6].

2. Scope of the Study

Recent findings from the global burden of disease (GBD) 2010 and 2013, studies have highlighted CKD as an important cause for global mortality. The number of deaths from CKD was estimated to be 9,56,200 in 2013, a 37 % increase from 1990, one of the largest increases among the top 50 causes of deaths, behind HIV/AIDS and diabetes. Thus, kidney disease constitutes a global public health priority, also underlined by the fact that worldwide the prevalence of end-stage renal disease (ESRD) patients receiving renal replacement therapy (RRT) with maintenance dialysis has increased 1.7 times from 165 patients per million population (pmp) in 1990 to 284 pmp in 2010. Moreover, it has been estimated that the projected number of people receiving RRT (dialysis or transplantation) will be more than double from 2618 million people worldwide in 2010 to 5436 million in 2030. Notably, between 2284 and 7083 million people who could have been kept alive with RRT in 2010 who had died prematurely because they did not have access to the treatment[11].

Chronic kidney disease (CKD) is a major public health problem.CKD was defined by a GFR < 60 ml/min per 1.73 m^2.In dialysis patients, cardiovascular disease (CVD) mortality rates are 10 to 30 times higher than in the general population. In high-risk patients, defined by the presence of either CVD or cardiovascular risk factors, less severe kidney disease is also an independent risk factor for CVD outcomes. Data from some studies suggest the absence of an independent association between the presence of CKD and CVD, whereas other data suggest that CKD is an independent risk factor for CVD outcomes[5].

The manifestations of cardiovascular disease in patients with chronic kidney disease are diverse. Studies have shown that even patients with mild kidney disease are at greatly increased risk for cardiovascular events.CVD and CKD have complex interactions and may produce metabolic imbalances such as chronic inflammation ,erythropoietin deficiency resulting anemia and metabolic disorder[8].

The higher death risk associated with CKD reflects higher rates of atherosclerotic vascular disease and congestive heart failure has clinical relevance. Kidney disease and cardiovascular disease both are approaching epidemic levels in the elderly. Both conditions seem to be lethally synergistic[9]. About 1 in 10 people have some degree of CKD. It can develop at any age and various conditions can lead to CKD.

It is estimated that about one in five men and one in four women between the ages of 65 and 74, and half of people aged 75 or more have CKD. In short, the older you get the more likely you are to have some degree of kidney disease. This is important because CKD increases the risk of heart attack and stroke, and in some cases can progress to kidney failure requiring dialysis or transplantation. Regardless of your age, simple treatments can slow the progression of kidney disease, prevent complications and improve quality of life[10].All stages of CKD are associated with increased risks of cardiovascular morbidity, premature mortality, and/or decreased quality of life. CKD is usually asymptomatic until later stages and accurate prevalence data are lacking.

Global mean of CKD prevalence of 5 stages were given as 13·4%, and stages III–V was 10·6%. CKD prevalence by stage was Stage I- 3·5% Stage II- 3·9%, Stage III-7·6%, Stage IV- 0·4% and Stage V- 0·1%. CKD has a high global prevalence with a consistent estimated global CKD prevalence of between 11 to 13% with the majority stage 3[11].

Kidney disease can affect people of all ages and races. African Americans, Hispanics, American Indians and people of South Asian origin (those from India, Bangladesh, Sri Lanka or Pakistan) have a higher risk of CKD. This risk is due in part to high rates of diabetes and high blood pressure in these communities.CKD can occur at any age, but becomes more common with increasing age. Although about half of people aged 75 or more have some degree of CKD, many of these people do not actually have diseases of their kidneys; they have normal ageing of their kidneys. Simple blood and urine tests can detect CKD and simple, low cost treatments can slow the progression of the disease, reduce the risk of associated heart attacks and strokes and improve quality of life.10% of the population worldwide is affected by chronic kidney disease (CKD), and millions die each year because they do not have access to affordable treatment[10].According the 2010 Global Burden of Disease study, chronic kidney disease was ranked 27th in the list of causes of total number of deaths worldwide in 1990, but rose to 18th in 2010. This degree of movement up the list was second only to that for HIV and AIDs[12]. Over 2 million people worldwide currently receive treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need treatment to live[13]. After the age of 40, kidney filtration begins to fall by approximately 1% per year. On top of the natural aging of the

kidneys, many conditions which damage the kidneys are more common in older people including diabetes, high blood pressure and heart disease.

Chronic Kidney Disease (CKD) is one of the major causes of death in India. Hypertension and Diabetes Mellitus are the common causes of CKD. Two studies showed significant correlation between CKD and age, Diabetes Mellitus, hypertension, serum creatinine. One study showed 23.5% of hypertensive subjects were having CKD stage III. Every year1,00,000 newly diagnosed patients of end stage renal disease (ESRD) start dialysis in India .From India limited data are available about the prevalence of CKD. In India diabetes and hypertension account for 40-60% cases of CKD. With increasing prevalence of these diseases in India, prevalence of CKD is expected to increase, and obviously this is the key target population to address. Identification of CKD in early stages is important to delay the progression of the disease which intern decreases the economic burden on individual, family and community. More such studies are required to sensitize the people about the functioning of kidney[14].

3. LITERATURE REVIEW

1. Bogdan Ene-Iordache et al did a crosssectional study on chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC). The study was conducted in 12 countries from six world regions: Bangladesh, Bolivia, Bosnia and Herzegovina, China, Egypt, Georgia, India, Iran, Moldova, Mongolia, Nepal, and Nigeria. Risk of cardiovascular disease development was estimated with the Framingham risk score. The number of participants at high risk of cardiovascular disease, according to the Framingham risk score, was underestimated compared with KDIGO guidelines. For example, all individuals with chronic kidney disease should be considered at high risk of cardiovascular disease, but the Framingham risk score detects only 23% in the general population, and only 38% in high-risk cohorts[15].

2. Yuichi Ikeda et al did a study on GDF15 [Growth differentiation factor] as a relative biomarker for cardiovascular risk assessment. The study shows GDF15 levels serve as an independent predictor of major cardiovascular diseases in Japanese patients with Acute Myocardial Infarction [AMI]. They had also reported that further studies are required to understand the pathophysiological roles in various cardiovascular diseases[16]

3. Steven C.Lin et al did a clinical trial study on cardiovascular risk assessment in the treatment of NASH [Non-Alcoholic Steatohepatitis] a secondary analysis of the MOZART [Magnetic Resonance Imaging and elastography in ezetimibe] for the assessment of response to treatment in NASH. The study was concluded that ezetimibe improved Framingham Risk Score and coronary artery calcification score which indicated the feasibility of monitoring CV risk in NASH trial as there were no much trials conducted [17].

4. Silvio E Inzucchi et al did a study on SGLT-2 [Sodium Glucose Co Transporter -2] Inhibitors and cardiovascular risk. The study revealed that cardiovascular risk was increased due to control Type2 Diabetes Mellitus and better glycaemic control was the lead factor. The study concluded that SGLT-2are novel oral glucose lowering agents and it reduce hyperglycemia in patients with T2 Diabetes Mellitus [18].

5. Vivian K. Kawai et al did a cross-sectional study in rheumatoid arthritis patients having increased cardiovascular risk. Coronary Artery Calcification have been increased in rheumatoid arthritis patients. The ACC/AHA risk score does not offer any advantage compared to the traditional FRS & RRS in identifying the risks in RA patients and it assigned almost 60% of patients with CAC to a low risk category. Risk scores and standard risk prediction models used in population which can't identify many RA patients with elevated cardiovascular risk [19].

6. Nisha Bansal et al done a prospective study on blood pressure and risk of all-cause mortality in advanced chronic kidney disease and hemodialysis - the chronic renal insufficiency cohort study. They studied the association between SBP and mortality when participants (1) had an estimated glomerular filtration rate <30ml/min/1.73m^2 (n=1705),(2) initiated hemodialysis and had dialysis – unit SBP measures and (3)initiated haemodialysis and had out-of-dialysis-unit SBP measured at a chronic renal insufficiency cohort study visit. At advanced chronic kidney disease, there was no association between SBP and mortality. Among participants who started hemodialysis, a U-shaped association between dialysis-unit SBP and mortality was observed. In contrast, there was a linear association between out-of-dialysis-unit SBP and mortality. In conclusion, more efforts should be made to obtain out-of-dialysis-unit SBP, which may merit more consideration as a target for clinical management and in interventional trials[20].

7. Paul M Ridker et al did an epidemiological study on High sensitivity C-reactive protein for Global risk assessment in the primary prevention of cardiovascular diseases and the protein's presence in plasma is the main risk and also a predictor for myocardial infraction, stroke, and vascular death in individuals without known cardiovascular disease. Overall increase in high sensitivity C-reactive protein increases the relative risk of suffering future cardiovascular event for both men and women [21].

8. J J Brugts et aldid a meta-analysis of randomized control clinical trial to understand the benefits of statins in people without established CVD but with CV risks. The

study concluded that patients without established cardiovascular disease but with cardiovascular risk factors use of statin and if had improved the survival and found to have a large reduction in the risk of cardiovascular events [22]

9. C W Siu et al did a study on pre-operative cardiac risk assessment in geriatric patients with hip fractures. The study revealed that risk assessment helps in not only identifying high risk patient before their operation and also reduces the unnecessary cardiac consultation for low risk patients [23].

10. Tanja Zeller et al did a study in high population of cardiac troponin I measured by a high sensitivity assay and cardiovascular risk estimation. The results provided evidence that high sensitive assayed troponin I is a cardiac-specific marker of global cardiovascular risk. It may reflect pathophysiological progression from myocardial health to myocardial damages [24].

11. Cláudia Bernardi Cesarino et al assessed the cardiovascular risk in patients with chronic kidney disease according to Framingham's criteria in a cross-sectional study with a sample of 242 patients with chronic kidney disease. The most prevalent risk factors for cardiovascular disease were: hypertension, sedentariness and smoking. Cardiovascular risk in relation to the variables gender and family income presented a statistical difference ($p<0.05$).This data showed low cardiovascular risk in patients with chronic kidney disease[25.]

12. Manish Bansal et al did a comparative study to differentiate risk scores in assessing cardiovascular risk in Indian patients with first myocardial infraction. Risk [WHO] underestimates the risk the most whereas Risk [FRS] and Risk [ACC/AHA] have intermediate accuracy. The study findings suggest that Risk [JBS] may be suited for Indians [26].

13. Holly C. Gooding et al did a study on cardiovascular risk assessment and cholesterol management in adolescents. They revealed that the major risk for cardiovascular disease was smoking, hypertension, hypercholesterolemia, diabetes and obesity. They concluded that risk assessment was very important for adolescent health [27].

14. Mona Razavian et al conducted a study on cardiovascular risk management in chronic kidney disease in general practice (the AusHEART study- Australian Hypertension and Absolute Risk Study. Among a total of 4966 patients with kidney function test data, 1845 (37%) had abnormal kidney function. The study concluded that among CKD patients not prescribed blood pressure- lowering agents or lipid-lowering agents, treatment was indicated as per relevant guidelines in 51 and 46%, respectively. For CKD patients who were already prescribed blood pressure-lowering and lipid-lowering agents, 61 and 50%, respectively, did not meet the treatment targets recommended by the relevant guidelines[28].

15. D S Prasad et al did a review about the association of smoking and cardiovascular health. They had concluded that tobacco use in India is complex and the burden was high and also it contributes to the pathogenesis of CVD. It also suggested that tobacco control is the most cost effective preventable cause of CV mortality and morbidity [29].

16. Sonal Parikh et al conducted a study on assessment of cardiovascular disease risk by using Framingham risk equation among the residence of Ahmedabad city. The study reported that the risk was higher in males especially in unskilled workers and was due to high use of tobacco and other executive group it was because of disease conditions like diabetes and obesity [30].

17. Z.Hambali et al conducted a study on oxidative stress and its association with cardiovascular disease in chronic renal failure patients. This study evaluated biomarkers of oxidative stress, NOx (total NO_2 and NO_3), and superoxide dismutase (SOD) enzyme in normal and CRF patients and correlated their association with CVD. However, it was noted that the levels of these biomarkers of oxidative stress were significantly lower in CRF patients with CVD compared with CRF patients without CVD. Therefore, these oxidative stress markers maybe contributing factors in the pathogenesis of CVD in patients with CRF[31]

18. Sigrun Halvorsen et al studied the aspirin therapy in primary cardiovascular disease prevention. In which thrombosis place an important role in acute cardiovascular disease and has resulted in a large number of clinical trials on the effectiveness of antithrombotic drugs in cardiovascular disease prevention. Thus the study revealed

that aspirin is the primary prevention of CVD in both sexes at a risk level of cardiovascular events [32].

19. Anping cai et al in their study on Lipoprotein associated phospholipase A_2 [LP-PLA2] as a novel and promising bio-marker for CV risk assessment. They concluded that A2 [LP-PLA2] appears to be a valuable biomarker for discriminating patients CV risk. And also could provide additive values of traditional risk factors in identifying a prone-rupture plaque [33].

20. Emanuele Di Angelantonio et al conducted a study on chronic kidney disease and risk of major cardiovascular disease and non-vascular mortality: prospective population based cohort study. 16958 people aged 33-81 years without manifest vascular disease and with available information on stage of chronic kidney disease (defined by both estimated glomerular filtration rate and urinary protein) at study entry. The study concludes that in people without manifest vascular disease, even the earliest stages of chronic kidney disease are associated with excess risk of subsequent coronary heart disease. Assessment of chronic kidney disease in addition to conventional risk factors modestly improves prediction of risk for coronary heart disease. Further studies are needed to investigate associations between chronic kidney disease and non-vascular mortality from causes other than cancer[34].

21. Meg J. Jardine et al conducted a study on aspirin is beneficial in hypertensive patients with chronic kidney disease. They used HOT (Hypertension Optimal Treatment) study were they randomly assigned participants with diastolic hypertension to aspirin (75 mg) or placebo. Study treatment effects were calculated using univariate proportional hazards. From the study they concluded that aspirin therapy produces greater absolute reduction in major cardiovascular events and mortality in hypertensive patients with CKD than with normal kidney function[35].

22. Anthony J. Viera et al in their review on global risk of coronary heart disease: assessment and application reported that coronary heart disease is the most common cause of death in the United States. The conventional risk factor approach to primary prevention excludes many patients who could benefit from preventive therapies. It is based on an empiric equation that combines major risk factors, such as blood pressure

and cholesterol levels. When physicians know a patient's global risk of coronary heart disease, they are more likely to prescribe risk-reducing therapies such as antihypertensives, statins, and aspirin. In addition, patients who know their risk level are more likely to initiate risk-reducing therapies. Many tools are available to estimate global risk, including several Web-based calculators. In the United States, tools based on the Framingham Heart Study are recommended[36].

23. Arvind Raghu et al did a study on implications of cardiovascular disease risk assessment using the WHO/ISH risk prediction charts in rural India. The study has demonstrated the differences in risk prediction of CV risks while using LI & HI models of WHO risk prediction charts [37].

24. Sharon Anderson et al evaluated chronic kidney disease prediction, progression and outcomes in older adults. It is summarized in this article, to review what is known about chronic kidney disease, identify research gaps and resources available to address them, and identify priority areas for future research. Answers to emerging research questions will support the integration of geriatrics and nephrology and thus improve care for older patients at risk for chronic kidney disease[38].

25. Lisa M Miller et al conducted a clinical cross sectional study on cardioprotective medication use in hemodialysis patients. The study reports shows that cardiovascular disease is the leading cause of mortality in patients with renal failure, accounting for more than 50% of deaths in end-stage renal disease. Risk factor modification with the use of cardioprotective medications such as angiotensin converting enzyme inhibitors (ACEIs), beta-adrenergic antagonists (beta-blockers), acetylsalisylic acid (ASA) and 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) has been shown to reduce mortality in the general population. The study reports that many hemodialysis patients were not prescribed with cardioprotective medications. The results of the study suggest that secondary prevention strategies are not widely adhered to in dialysis patients. Each class of medications was prescribed to less than one-half of the entire cohort[39].

26. Jeffrey Brinker critically assessed cardiovascular risk in patients with chronic kidney disease. Studies have shown that even patients with mild kidney disease are greatly

increased risk of cardiovascular events. Patients with CKD should be assessed for coronary artery disease by traditional screening procedures as well as non tradional screening procedures such as C - reactive protein, homocysteine determinations. Reliable indicators for early kidney disease such as estimated creatinine clearance are perhaps underutilized in identifying patients who have increased cardiovascular risk as a result of renal insufficency[8].

27. Robert N. Foley et al studied chronic kidney disease and risk for cardiovascular disease, renal replacement, and death in the United States among medicare population. Knowledge of the excess risk posed by specific cardiovascular syndromes could help in the development of strategies to reduce premature mortality among patients with chronic kidney disease (CKD).On a relative basis, patients with CKD were at a much greater risk for the least frequent study outcome, renal replacement therapy. On an absolute basis, however, the high death rates of patients with CKD may reflect accelerated rates of atherosclerotic vascular disease and congestive heart failure[9].

4. OBJECTIVES OF THE STUDY

The study entitled **"Assessment and Prevention of risk for development of Cardiovascular diseases in Geriatric population with Chronic kidney disease"** was aimed to achieve the following objectives:

1. To assess the next 10 year risk for cardiovascular events in patients with chronic kidney disease using QRISK calculator, Framingham's risk score and WHO charts.
2. To compare the risks obtained from three scales.
3. To provide prevention strategy for the patients with chronic kidney disease for their cardiovascular risk.
4. To assess the prescription patterns for patients with chronic kidney disease.

5. PLAN OF THE STUDY

The study entitled **"Assessment and Prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease"** was planned and carried out as given below:

Phase 1 :- (December 2015 to January 2016)

- Literature survey to identify the scope of the work
- Submission of protocol and obtaining consent from hospital authority.
- Designing of:
  - ✓ Data entry format
  - ✓ Patient information and consent form
  - ✓ Inclusion and exclusion criteria for data collection.

Phase 2 : - (February to July 2016)

- Data collection through standard data entry format in ward rounds.
- Literature survey (continued)
- Data analysis.

Phase 3:- (August 2016)

- Literature survey (continued)
- Application of statistical tool on the obtained data.
- Preparation and submission of reports.

6. METHODOLOGY

Study Site

The study was conducted at a private tertiary care hospital at Coimbatore. It is a 750 bedded multi-specialty institution, one of the largest hospitals at Coimbatore. The hospital is unique and people from all over the country come and avail its facilities. The various specialties include General Medicine, Obstetrics and Gynecology, Pediatrics and Neonatal, Neurosciences, Anesthesiology, Orthopedics, Radiology, Nephrology, Pulmonology and Critical Care, Cardiology and Cardiothoracic surgery, Microbiology, Pathology and Hematology, Laparoscopic surgery, ENT, Dental and Maxillofacial surgery, Neurology, Ophthalmology, Physical Medicine and Rehabilitation, Diabetology, Surgical Gastro Enterology, Oncology. The hospital is also equipped with the modern diagnostic facilities like CT scan, MRI scan, PET scan, Ultra Sound Sonography, Digital Subtraction Angiography, ECG, Treadmill, Colour Doppler etc. The hospital also has twelve hi-tech operation theaters, Intensive Care Unit, Intensive Cardiac Care Unit, Intensive Pulmonary Care Unit, Catheterization, Balloon Valvuloplasty, Coronary stenting, Kidney transplantation unit with Haemodialysis machines and an assisted Reproductive Technology Centre. 24 hrs microbiological, blood bank, pathological services, round the clock causality and pharmacy services etc

Department selected for study in the hospital

The study was conducted in the department of Nephrology and general medicine. The reason for the selection of this department was that the pilot study revealed more scope for the study in the department of Nephrology. The prevalence of chronic kidney disease were found to be more and the department of pharmacy practice provides service to the above department and a good co-operation from medical team added up as a reason for selecting the department for conducting the present study. The study was conducted with expert guidance of the Clinical Pharmacy Professionals and Physician from nephrology department.

Consent from the hospital authorities

It is mandatory that every project work carried out in the hospital by the M. Pharmacy (pharmacy practice) student has to be approved by the Institutional Ethical Committee of hospital. A protocol of the study which includes the objectives, methodology, and probable outcomes was prepared and submitted to the Institutional Ethical Committee of

the study hospital. The approval from the committee was procured through the letter **[SRH/EC.5-7/2016-17 dated 26TH February 2016]** and the same was given in **Annexure No.1**for reference. The study was conducted with the expert guidance of senior and junior physicians of the departments selected. The author was permitted to utilize the hospital facilities to make a follow up of the cases, in the selected departments. All the health care professionals of the study site were well informed through Dean's official circular.

Literature survey

Literature survey was done in order to collect the supporting evidence for the study proposed and this has been continued throughout the study period to update the knowledge about the topic and other related areas. The necessary information from the literatures were collected and well documented. The literatures supporting the study were gathered from various sources such as:

- Journal of the American society of nephrology
- British Medical Journal
- American heart association journals
- Canadian journal of cardiology
- Journal of the American College of Cardiology
- Nephrology Dialysis Transplantion
- Lancet global Health
- American Academy of Family Physicians
- International Education & Research Journal
- Internship emergency medicine
- Kidney international journal
- Indian journal of nephrology

IOWA Drug Information Services (IDIS), a database released by the College of Pharmacy, University of IOWA, Micromedex, Medscape, Pub med, Science direct and other databases were also been widely used.

The following were some of the textbooks used for references were,

1.Joseph. T. Dipiro, Pharmacotherapy-A pathological Approach by 7th edition (2008); pg. no.619-624.

2.Roger Walker and Cate Whittlesea; Clinical Pharmacy and Therapeutics; 5th edition (2012); pg.no.213-220,132-140.

3.K.D. Tripathi. Essentials of medical pharmacology; 6th edition; pg. no. 667-808.

4.Mohsen Ziai M.D; Pediatrics; 3rd edition; pg.no. 1-5.

Design of patient informationform

A patient information form has been prepared, to inform the care givers of patients about the purpose, necessity of the study and assuring them that the confidentiality will be strictly maintained and this is for only the betterment of patient's health. The format includes the details like Department address, name and signature of the investigator and supervisor, date, place and details of the study. The model of the patient information form was given in the **Annexure No.: 2** for reference.

Design of patient consent form

A patient consent form has also been prepared to obtain written consent from all the patient or bystander and will be included in the study. They will be informed about the study using patient consent form. The format contains details like address, date, place, provision for signature of the patient or bystander, investigator and supervisor. The same was given in the **Annexure No.: 3** for reference.

DESIGN OF DATA ENTRY FORM

A separate data entry form for incorporating patient details were designed and the format contains provision to enter the details such as name, age, sex, height, weight, IP. No, date of admission, date of discharge, vital signs, reason for admission, past medical history, past medication history, and any predisposing factors. Provision was given in the format for entry of details like blood counts, liver function test, renal function test, pulmonary function test, electrolytes, urine examination, diagnosis, drug chart, and drug interaction chart and dose and any interventions. The model of the patient Data entry form was given in the **Annexure No.: 4** for reference.

Inclusion criteria: All in-patients of age above 64 years of either sex admitted into the study site during the study period, who have been diagnosed to have chronic kidney disease with

serum creatinine measurement and are willing to participate will be included in the study.

Exclusion criteria: Patients, younger than 65 years, patients with no serum creatinine measurement or with insufficient data, critically ill, out-patients and who were not willing to participate were be excluded from the study.

Data collection

Data were collected during a regular ward round participation in the department of Nephrology and general medicine. Patients who had satisfied the inclusion criteria were included. Patient or care givers were informed about the study and their written consent was obtained from them, using appropriate forms. Data collection form was used to obtain information on demographics of patient (e.g. Patient name, age, gender, height, weight, data of admission and date of discharge), presenting complaints, provisional/ confirmed diagnosis, drug therapy given (with brand name and generic name of each drug, dose, duration and route of therapy) and laboratory test reports.

Data analysis

Prospective observational cross sectional study was used to assess cardiovascular risk for next 10 years in patients with chronic kidney diseases. Data concerning to patients' socio-demographic and economic profiles, will be collected through interviews from patients and consultation of medical files to obtain clinical, laboratory and anthropometric data. The collected data was analysed using Microsoft Excel spreadsheet. Frequency tables were used for the categorical variables (gender, age, diabetes and hypertension) and descriptive statistics (average, standard deviation) for the continuous variables. The Chi-square test was used for the analysis of association among the following variables: risk factors, gender, and age at a level of significance of $p<0.05$ was adopted.

The Framingham Risk Score[25] was be used to assess cardiovascular risk. The same was given in the **Annexure No.:5** for reference. The total score takes into account the following variables: gender, age, smoking, diabetes mellitus, high-density lipoprotein, total cholesterol, systolic blood pressure and diastolic blood pressure. The score obtained corresponds to the likelihood of cardiovascular diseases occurring in the next ten years, expressed as a percentage. Hence, the individuals were classified in the following categories:

low risk, which refers to a probability lower than 10% of cardiovascular events occurring in ten years; average risk, between 10% and 20%; and high risk, greater than 20%[7].

The results were analysed by means ofQRISK®2 a well-established cardiovascular disease (CVD) risk score, which is designed to identify people at high risk of developing CVD who need to be recalled and assessed in more detail to reduce their risk of developing CVD. The QRISK®2 score estimates the risk of a person developing CVD over the next 10 years.QRISK®2 has been specifically developed by doctors and academics for use in the UK.The original research underpinning QRISK® was published in July 2007 in the British Medical Journal and in January 2008 in Heart journal[40]. The original research underpinning version 2 of QRISK® (QRISK®2) has been published in the British Medical Journal in June 2008[40].The research was done using the QResearch anonymised medical research database which consists of the electronic health records of over 10 million patients registered with 550 general practices using the EMIS clinical computer system of whom 2 million contributed to the Q Research database.

The results were also analysed through WHO charts. These charts indicate 10-year risk of a fatal or non-fatal major cardiovascular event (myocardial infarction or stroke), according to age, sex, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus for 14 WHO epidemiological sub-regions. The charts provide approximate estimates of cardiovascular disease (CVD) risk in people who do not have established coronary heart disease, stroke or other atherosclerotic disease. The WHO charts was given in **Annexure No.6** for reference. They are useful as tools to help identify those at high cardiovascular risk, and to motivate patients, particularly to change behaviour and when appropriate to take antihypertensive, lipid-lowering drugs and aspirin.

7. RESULTS

The study entitled **"Assessment and Prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease"** has the following results. Data were collected from the study population of 102 geriatric patients who had fulfilled the inclusion criteria. The obtained data were analyzed and the results were given in the following sections.

Prevalence of CKD:

The study site had 1667 patients admitted during the study period. There were 102 patients included in the study as they matched the inclusion and exclusion criteria of the study. Hence the prevalence of chronic kidney disease among the geriatrics was 6.1%. The prevalence details are given below.**Tab.No.5**

Tab.No.5:- Prevalence of CKD patients

S.No.	Description	Number of Patients	% Patients
1.	**Patients who were not included in the Study**	**1565**	**93.9%**
2	**Patients included in the study**	**102**	**6.1%**

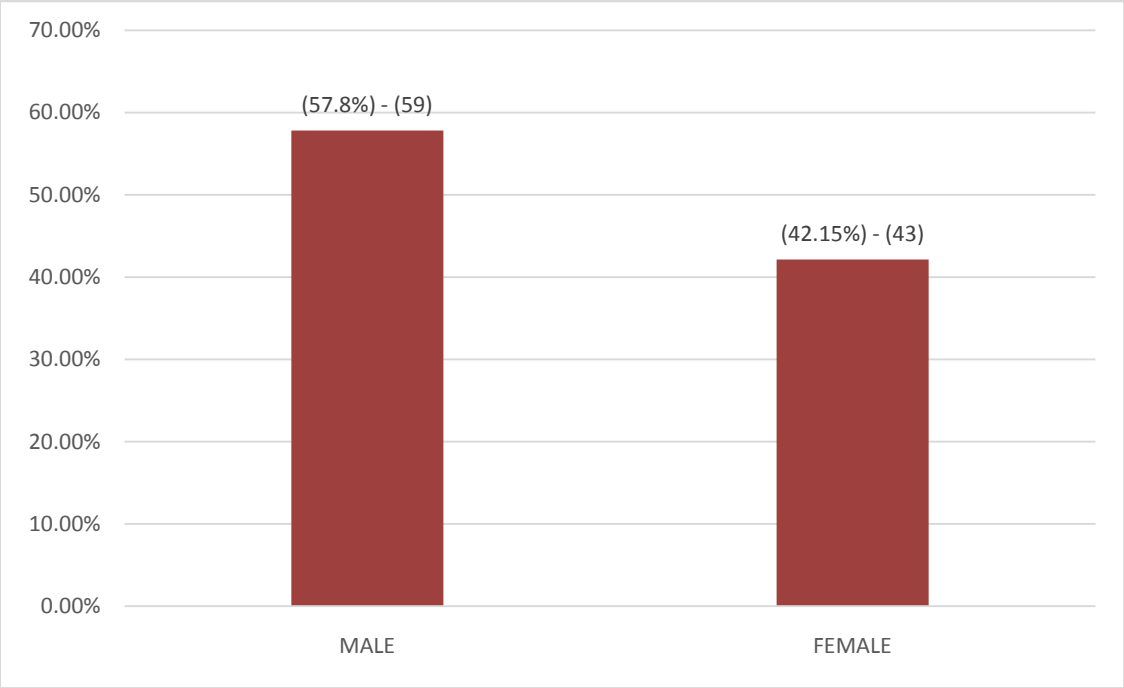
Gender distribution

The study results revealed that a predominant male population of 57.84% was observed among the study population and the same was depicted in **Fig. No: 5.**

Age Distribution

The study population was categorized into young or new elderly (65-74), old elderly (75-84), oldest old (>84).Age distribution of the study population was analyzed and it was found that 85.29% were in the age group 65-74 years in which males were 89.83% and females 79.06%. The details of the age distribution of the study population were given in **Tab. No.6.**

Fig. No. 5: - Gender distribution (n=102)



Tab. No.6: - Age categorisation of study population (n=102)

Age group	Percentage Male (No.) (n=59)	Percentage Female (No.) (n=43)	Over all percentage(No.) (n=102)
65 to 74years (New elderly)	89.83(53)	79.06(34)	85.29(87)
75-84 years (Old elderly)	7.54(4)	18.60(8)	11.76(12)
> 84 years (oldest old)	3.77(2)	2.32(1)	2.94(3)

Body Mass Index (BMI)

The Body Mass Index of the study population was calculated by using weight and height of the patient. The BMI were calculated using the following formula:

BMI = weight in kilograms / height in meters^2

As the BMI is a modifying risk factor for an individual to have cardiovascular risk and thus the classification becomes very important. Results revealed that 20.54% of the study population were having greater BMI value than normal and also at high risk category for getting cardiovascular disease in future. It also reveals that 79.40% were very well normal and do not have the risk. The details were given in **Tab.No.7.**

Tab. No.7: - Body mass index (n=102)

Category	Value	Percentage Males(No.) (n=59)	Percentage Females(No.) (n=43)	Over all percentage(No.) (n=102)
Severe thinness	<16	---	----	
Moderate thinness	16 to17	----	----	----
Mild thinness	17 to 18.5	16.94 (10)	11.62(5)	14.70(15)
Normal	18.5 to 25	62.71(37)	67.44(29)	64.70(66)
Over Weight	25 to 30	16.94(10)	18.60(8)	17.64(18)
Obese class I	30 to 35	1.69(1)	----	0.98(1)
Obese class II	35 to 40	1.69(1)	2.32(1)	1.92(2)

Length of Stay

Length of stay of study population in hospital were analyzed and the results were given in **Tab. No.8.**It was found that 55.87% of study population had atleast for minimum6 days in the hospital. This analysis had given an insight of the cost incurred for the treatment which would be generally high if the number of days stay is going to be more. The minimum number of days of hospital stay for the study population was found to be 2 days and maximum 15 days. The average number of days of hospital stay was found to be5.470 $\pm$ 2.639 days

Tab. No.8:- Length of stay (n=102)

Days	Percentage(No.)
<3	13.72(14)
3 to 5	30.39(31)
6 to 8	32.35(33)
9 to 10	15.68(16)
>10	7.84(8)

Reasons for Admission

The analysis of reasons for admission to the study site had revealed that certain complaints like difficulty in breathing, vomiting, swelling of limbs, decreased urine output etc., were found to be very common. The details of the complaints were given in **Tab. No.9.**

Past Medical History

The past medical history of the study population was also analyzed and the data were available with only few patients. The details were given below **Tab. No.10** Results revealed that diabetes mellitus, chronic renal failure and hypertension were very prevalent among the study population.

Tab. No.9:- Reasons for admission (n=102)

S. No.	Complaints	Percentage(No.)
1	Difficulty in breathing	32.35(33)
2	vomiting	16.66(17)
3	Swelling of limb	15.68(16)
4	Decreased urine output	14.70(15)
5	Fever	12.74(13)
6	Decreased appetite	7.84(8)
7	Nausea	6.86(7)
8	Loose stools	6.86(7)
9	Fatigue	6.86(7)
10	Elevated renal parameters	5.88(6)
11	Back pain	5.88(6)
12	Cough	4.90(5)
13	Slurry of speech	3.92(4)
14	Ulcer	3.92(4)
15	Headache	3.92(4)
16	Knee pain	2.94(3)
17	Leg swelling	1.96(2)
18	Diarrohea	1.96(2)
19	Chest pain	1.96(2)
20	Giddiness	1.96(2)
21	Weight loss	0.98(1)

Tab.No.10:- Past medical history

S. No.	Diseases	Percentage(No.)
1	Diabetes mellitus	50(51)
2	Chronic renal failure	32.35(33)
3	Hypertension	28.43(29)
4	Asthma	5.88(6)
5	Hypothyrodism	3.92(4)
6	COPD	1.96(2)
7	Parkinson's disease	0.98(1)
8	Liver Cirrhosis	0.98(1)

Past Medication History

The details about the past medication history of study population was also done and details were available with only few and given below **Tab.No.11.**

Tab.No.11:-Past medication history

S. No.	Drugs	Percentage(No.)
1	Insulin	13.72(14)
2	Amlodipine	12.74(13)
3	clinidipine	9.80(10)
4	Glimipride	8.82(9)
5	Telmisartan	7.84(8)
6	Atorvastatin	4.90(5)

Family History

The analysis of family history of having any of the disease conditions becomes more important as this is one of the non –modifying risk factor of having cardiovascular disease was family history. The details of having of such analysis are given in **Tab.No.12**

Tab.No.12:-Details of family history

Sl. No.	Disease	Percentage(No.)
1	Diabetes mellitus	32.35(33)
2	SHT	20.5(21)
3	CRF	1.96(2)

Social History

The individual habit reluctant to taking of alcohol and tobacco becomes an important risk factor for most of clinical condition in this regard 79.4%of study population didn't have the risk of having cardiovascular risk because they do not have the habit of smoking or drinking of alcohol. The details were given below in the **Tab.No.13**

Tab.No.13:- Social history

Sl. No.	Social habits	Percentage(No.)
1	None	79.4(81)
2	Alcoholic	1.96(2)
3	Tobacco	18.62(19)

Laboratory Investigations

The laboratory investigations for the study population were given below **Tab. No: 14.** The result had revealed that electrolytes serum creatinine, urea, and GFR were commonly assessed to most of the study population as it has included CRF patients.

Tab. No: 14: - Laboratory investigation (n=102)

Sl. No.	Investigations	Percentage(No.)
1	Electrolytes	100(102)
2	Serum creatinine	100(102)
3	Urea	97(99)
4	GFR	96.07(98)
5	Hemoglobin	88.23(90)
6	WBC	86.27(88)
7	CNS	76.47(78)
8	CVS	73.52(75)
9	Platelet	63.72(65)
10	Temperature	58.82(60)
11	Blood glucose	49.01(50)
12	Liver function test	41.76(42)
13	RBC	38.23(39)
14	Lipid profile	14.70(15)
15	ESR	9.80(10)
16	Echo	1.96(2)
17	endoscopy	1.96(2)
18	epithelial	0.98(1)

Diagnosis

The provisional diagnosis of the study population was also analyzed and the common diagnosis was found to be systemic hypertension, diabetes mellitus, chronic renal failure, etc. The details were given below **Tab. No.15.** Results revealed that the modifying variable risk factors other than CRF, systemic hypertension, diabetes mellitus and renal failure were also very prevalent among the study population. In general anemia will be more common in CRF patient which is also evident in the study population.

Tab. No.15: - Diagnosis (n=102)

S. No.	Diseases	Percentage(No.)
1	CRF & other related disease	100(102)
2	Diabetes mellitus	38.23(39)
3	Hypertension	22.54(23)
4	Anaemia	18.62(19)
5	Bronchial asthma	5.88(6)
6	Hypothyroidism	4.90(5)
7	UTI	2.94(3)
8	Renal stone disease	2.94(3)
9	Hyperkalemia	2.94(3)
10	COPD	1.96(2)
11	Acute pulmonary edema	1.96(2)
12	Renal biopsy	1.96(2)
13	Global hyperkinesia	1.96(2)
14	Liver cirrohsis	1.96(2)
15	Acute gastroenteritis	1.96(2)
16	Alcohol hepatitis	1.96(2)
17	Seizure disorder	0.98(1)
18	Parkinson’s disease	0.98(1)
19	Glomerular nephritis	0.98(1)
20	Migraine	0.98(1)

Drug Categories

The drugs used in study population were analyzed and the list of drugs prescribed was shown in **Tab. No: 16.** Analysis revealed that majority of the study population has received anti-hypertensive and antibiotics and proton pump inhibitors. And almost majority of population has received one or more vitamin supplements. The average was found to be 8.009±2.852.The maximum number of drugs given to patient is 14 and minimum is 3.

Tab. No: 16A – Drug categories (n=102)

S.No.	Drugs category (%) n=817	Name of the drug	Percentage(No.) n=102
1	Vitamins and mineral(30.50)	calcitrol	53.9(55)
		Calcium acetate	47.05(48)
		Folic acid	42.1(43)
		Vitamin supplements	30.3(31)
		alfacalcidol	16.6(17)
		Alpha glutaanalogue	13.7(14)
		Methylcobalamin	9.8(10)
		iron	9.8(10)
		calcium	8.82(9)
		Multivitamins	5.8(6)
		Pregabalin	3.9(4)
		Biotin	0.98(1)
2	Anti-hypertensives (11.31)	Clinidipine	37.2(38)
		Metoprolol	10.7(11)
		Nebivolol	10.7(11)
		Prazocin	8.82(9)
		Amlodipine	5.8(6)
		Atenolol	3.92(4)
		Moxonidine	3.92(4)
		Losartan	3.92(4)
		Clonidine	1.92(2)
		Naftopidil	1.92(2)
		Alfazocin	0.98(1)
3	Antibiotics (9.59)	Piperacillin sodium+tazobactum	19.6(20)
		Pre -probiotics	13.7(14)
		Cefalosporins	12.7(13)

		Penicillin	7.8(8)
		Amoxicillin+clavulanic acid	7.8(8)
		Cefixime + sulbactam	2.9(3)
		Ornidazole	2.9(3)
		Imepenam+cilastin	1.9(2)
		Ofloxacin	1.9(2)
		Macrolides	1.9(2)
		Garamycin	0.98(1)
		Ceftriazone	0.98(1)
		Levofloxacin	0.98(1)
4	Proton pumb inhibitor (9.10)	Pantoprazole	67.6(69)
		esomeprazole	4.9(5)
5	Anti anginal drugs(6.64)	Atorvastatin	23.5(24)
		Isosorbide mononitrate	11.7(12)
		Nicorandil	4.9(5)
		Levocarnitine	3.92(4)
		Amlodarone	2.92(3)
		Trimetazidine	2.9(3)
		Digoxin	1.92(2)
		Rosuvastatin	0.98(1)
6	Diuretics (3.19)	Torsemide	21.5(22)
		Furosemide	1.92(2)
		Spirolactone	1.92(2)
7	Anti – hyperurisemia(3.19)	Febuxostat	25.4(26)

Tab. No: 16B – Drug categories (n=102)

Sl.No.	Drugs category (%) n=817	Name of the drug	Percentage(No.) n=102
1	Anti –emetics (2.95)	Ramosetron	18.62(19)
		Ondansetron	3.9(4)
		Metoclopramide	0.98(1)
2	Anticoagulants (2.33)	clopidogrel	8.8(9)
		Asprin+clopidogrel	7.8(8)
		warfarin	1.9(2)
3	Analgesics (2.21)	Paracetamol	17.6(18)
4	Antidotes (2.09)	sevalmer	10.7(11)
		Acetyl cysteine	5.7(6)
5	Hypoglycemic agents (2.09)	Insulin	11.7(12)
		Glimipride	0.9(1)
		Linagliptin	0.9(1)
		Sitagliptin	0.9(1)

6	Hormones (2.09)	Methyl prednisolone	8.82(9)
		Levothyroxine	3.9(4)
		Erythropoietin	1.92(2)
7	Antiepileptics (2.09)	Clobasam	4.9(5)
		Mecobalamine	2.9(3)
		Piracetam	2.92(3)
		Flunarazin	1.92(2)
		Citicoline	0.98(1)
		Diazebam	0.98(1)
8	Antacids (1.59)	Sodium bicarbonate	6.8(7)
		Pantoprazole+domperidone	3.92(4)
		Famotidine	1.92(2)
9	Anti-diarroheals (1.23)	Vibact	8.8(9)
		Racecodril	0.92(1)
10	Anti-asthmatics (1.10)	Etophylline+theophylline	5.8(6)
		Acebrophylline	2.9(3)
11	Anti-inflammatory agents(1.10)	Tramadol	3.9(4)
		Chymotrypsin	2.9(3)

Tab. No: 16 C – Drug categories (n=102)

Sl.No.	Drugs category (%) n=817	Name of the drug	Percentage(No.) n=102
1	Hepatic protectors (0.98)	Ursodeoxycholic acid	7.8(8)
2	Anti vertigo(0.98)	Betahistine	5.8(6)
		meclozine	1.9(2)
3	Anxiolytics (0.86)	Hydroxyzine	2.9(3)
		Alprazolam	2.92(3)
		Clonotril	0.96(1)
4	Haemotropic (0.73)	Darbepoetin alpha	4.9(5)
		Transeamic acid	0.9(1)
5	Anti tussives (0.49)	bromohexine	1.9(2)
		levocloparasitine	1.9(2)
6	Immunosupprasants (0.49)	Tarcolimus	1.9(2)
		Azathioprine	1.9(2)
7	Anti-fungal (0.49)	Fluconazole	3.9(4)
8	Anti-malarials (0.36)	HCQS	2.92(3)
9	Appetite enhancer (0.36)	Elixir neogardine	2.9(3)
10	Laxatives (0.24)	Liquid paraffin	1.92(2)
11	Sedatives (0.12)	Zolpedem	0.92(1)
12	Anti tuberculosis (0.12)	Ethambutol	0.92(1)

Route of Administration

Route of administration of the prescribed drugs to the study population was analyzed. The detail of route administration was given in **Tab. No. 17&17 A.** The analysis had revealed that about 83.33% of patients had received injectables prescribed and that accumulated to about 22.64% of total drugs that were given as injection to the study population.

Tab. No.17: - Route of adminstration of drugs (n=102)

Route	Percentage(No.)
Oral	100(102)
Injectable	83.33(85)

Tab. No. 17A: - Route of adminstration of drugs (n=817)

Route	Percentage(No.)
No . of Oral drugs	77.35(632)
No. of Injectables	22.64(185)

STAGES OF KIDNEY DISEASE

The various stages of kidney disease was analysed and found that only 10% of population belongs to stage I and II and rest where above stage III. The results were given in **Tab.No.18.**

Tab.No.18:- Stages of kidney disease

Stages	Percentage Male (No.) (n=59)	Percentage Female (No.) (n=43)	Over all percentage(No.) (n=102)
Stage I	1.69(1)	4.65(2)	2.94(3)
Stage II	6.77(4)	11.62(5)	8.82(9)
Stage III	52.54(31)	41.86(18)	48.03(49)
Stage IV	22.03(13)	23.25(10)	22.54(23)
Stage V	16.94(10)	18.60(8)	17.64(18)

The prevalence of haemodialysis patient among study population was analysed. It was found 30.29% of them had undergone haemodialysis and majority of the population was non-hemodialysis patient. The patient undergoing hemodialysis were belong to stage IV and stage V.

CARDIOVASCULAR RISK ASSESSMENT

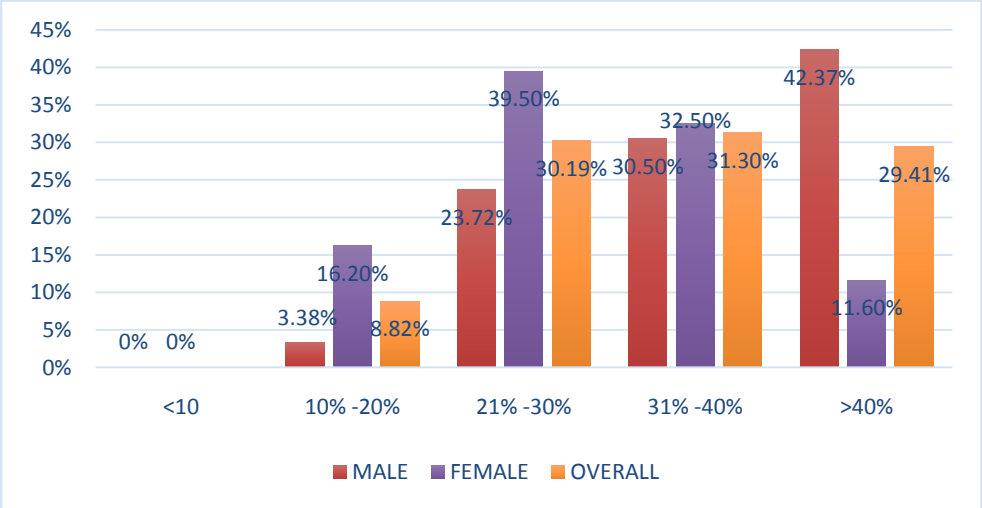
QRISK Scale Risk Assessment

The 10 year risk was assessed through QRISK calculator. Results had revealed that 29.41% of the study population were been categorised in the risk level of ≥40% in which 42.37% were males and 11.6% were females. The detail are given below **Tab no.19& Fig no.6**

Tab. No. 19:– Q-RISK Assessment (n=102)

Risk Level	Percentage of Males(No.) (n=59)	Percentage of Females(No.) (n=43)	Over all Percentage(No.) (n=102)
<10%	-	-	-
10 to 20%	3.38(2)	16.2(7)	8.82(9)
21 to 30%	23.72(14)	39.5(17)	30.19(31)
31 to 40%	30.50(18)	32.5(14)	31.3(32)
≥40%	42.37(25)	11.6(5)	29.41(30)

Fig.No.6:- Q-RISK assessment (n=102)



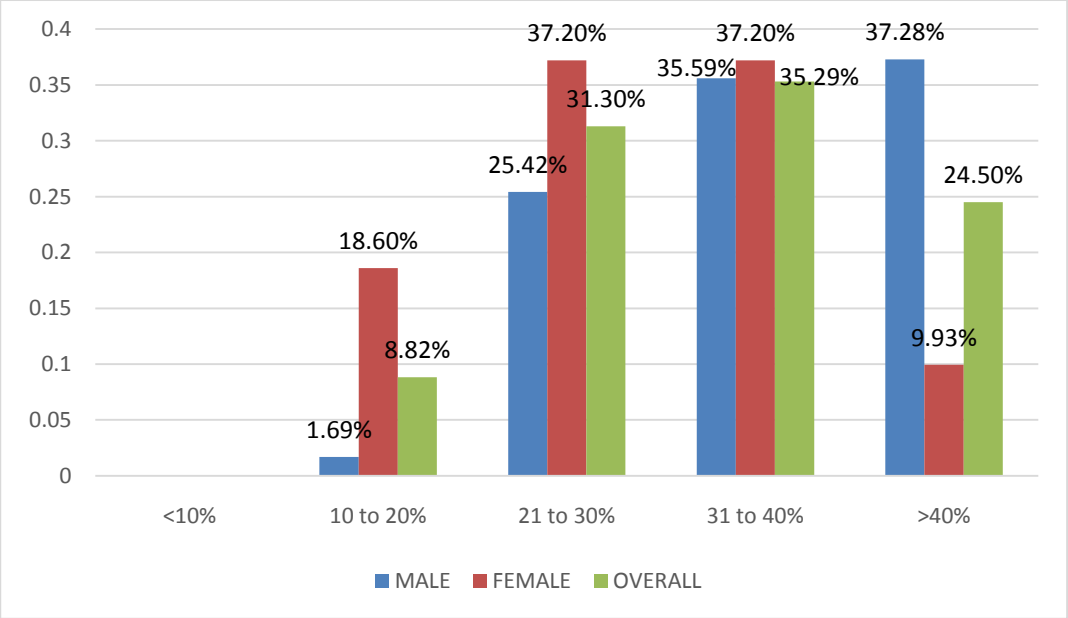
Framinghams Risk Assessment

The Framingham Risk Score is a gender-specific algorithm used to estimate the 10 year cardiovascular risk of an individual. The Framingham Risk Score was first developed based on data obtained from the Framingham Heart Study, to estimate the 10-year risk of developing coronary heart disease. The datas were analysed using Framingham risk calculator and it was found that 24.50% of population were at high risk in which males were 37.28% and females were 9.93%.the details were given below **Tab No.20 and Fig.No.7.**

Tab. No.20:- Framinghams Risk Assessment

Risk Level	Percentage of Males(No.) (n=59)	Percentage of Females(No.) (n=43)	Over all Percentage(No.) (n=102)
<10%	-	-	-
10 to 20%	1.69(1)	18.60(8)	8.82(9)
21 to 30%	25.42(15)	37.20(16)	31.3(32)
31 to 40%	35.59(21)	37.20(16)	35.29(36)
≥40%	37.28(22)	9.93(4)	24.50(25)

Fig No.7:- Framinghams risk assessment



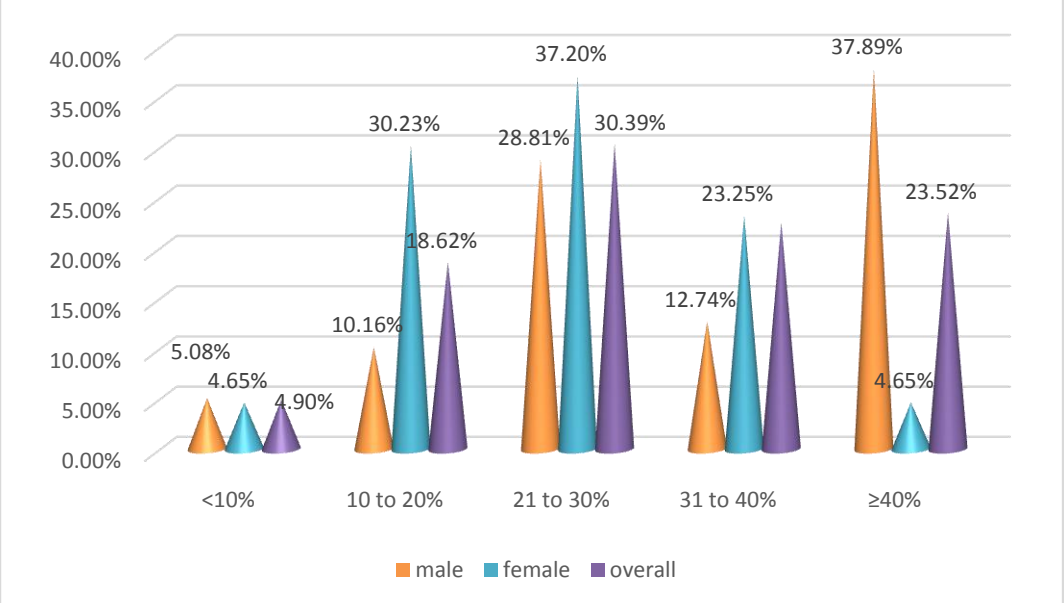
WHO Scale Risk Assessment

The cardiovascular risk assessments of the study population obtained by using WHO scale were given in **Tab. No.21 and Fig. No: 8.** Result had revealed that 28.43% of the study population were been categorised in the risk level of ≥40% in which 33.89% were males and 4.65% were females. An overall 4.90% study population only were having risk of level less than 10%.

Tab. No. 21:- WHO Scale Risk Assessment

Risk level	Percentage of Males(No.) (n=59)	Percentage of Females(No.) (n=43)	Over all Percentage(No.) (n=102)
<10%	5.08(3)	4.65(2)	4.90(5)
10 to 20%	10.16(6)	30.23(13)	18.62(19)
21 to 30%	28.81(17)	37.20(16)	30.39(31)
31 to 40%	12.74(13)	23.25(10)	22.54(23)
≥40%	37.28(22)	4.65(2)	23.52(24)

Fig. No.8:- WHO scale risk assessment



Comparison of the Risk Scales

Comparison of the risk assessment by different scales had revealed that WHO scale using chart values has categorised 4.9% of the study population into very low or no risk category where the other scales didn't categorise anyone in that category but in the very high risk category all the three scales were able to categorise more or less similar difference in the result. The use of QRISK calculator was reported to be more accurate and use WHO charts. The result also revealed a similar number between QRISK and Framingham's in all the categories of risk level but WHO scale differs[38].The details of comparison is given below **Tab.No.22**

Tab.No.22:- Comparison of the Risk Scales

Risk level	Risk score	QRISK	Framingham's score	WHO scale
No risk	<10%	-	-	4.90(5)
Low risk	10 to 20%	8.82(9)	8.82(9)	18.62(19)
Moderate risk	21 to 30%	30.19(31)	31.3(32)	30.39(31)
Light risk	31 to 40%	31.3(32)	35.29(36)	22.54(23)
Very high risk	≥40%	29.41(30)	24.50(25)	23.52(24)

Drug Related Problems

The analysis of drug related problems in the prescription given to the study population had revealed the following DRP's. The details were shown below in **Tab.No. 23.**

Tab.no.23:- Drug Related Problems

Sl.No.	Drug Related Problems	Drugs	Problems	Interventions
1	Dosage adjustment	Inj.tazar (pipercillin+tazobactum	4.5gm is given bd	2.25 gm is the recommended dose for renal impairment patients
		Tab.aldactone (spirolactone)	50mg	25 mg orally once daily
2	Drugs prescribed without indication	Inj. Vitamin K	It is prescribed for coagulation	It can be avoided.
		Tab.Abphylline sr	The drug was prescribed for asthma	It can be avoided.
		Tab.storvas	The drug was prescribed for hypertension	It can be avoided.
3	No drugs for indication	Bronchial asthma	Drugs was not prescribed	Tab. Deriphylline 100mg bd can be given.
		COPD	Drugs was not prescribed	Tab. Deriphylline 100mg bd can be given.
		Hyperuresemia	Drugs not prescribed	Tab.Febuxostat40 mg bd can be given
		Hypothyroidism	Drugs not prescribed	Tablet thyronorm 50mcg can be given
4	Therapeutic duplication	Inj.pan and tab.pantocid was precribed	Affects therapeutic efficacy	Inj.pan may be avoided
		Inj.pan and tab.sompraz d	Synergestic effect	Inj .pan may be aavoided

Drug Interactions

The analysis of drug-drug interaction prevailing in the prescriptions of study population had revealed that 44.11% of prescriptions were having one or more interaction and rest 55.88% didn't have even one drug-drug interaction. There were about 21 drug-drug interactions prevailing in the prescriptions of study population which account of a drug – drug interaction. The average was found to be 0.6568 ± 0.969.The details of the number of interactions were given in **Tab. No.24.**

Tab. No.24: - Drug interaction Categorisation (n=102)

Drug interactions	Percentage(No.)
No interaction	55.88(57)
One interaction	21.56(22)
Two interaction	12.74(13)
Three interaction	4.90 (5)

The **Tab. No.24A: - 24C** will be giving the details of drug-drug interactions prevailing in the prescription.

Tab. No. 24A: - Major Drug Interactions

Precipitant Drug	Interacting drug(No.)	Effect	Inference
Warfarin	Piperacillin + tazobactam (3)	Increased risk of bleeding	Monitoring of patients INR is recommended
	Torasemide (4)	Increased warfarin concentration, decreased warfarin clearance, elevated INR	Adjust warfarin dose
Amlodipine	Clopidogrel (2)	Decreased anti-platelet effect, Increased risk of thrombotic events	Monitor patient for loss of clopidogrel efficacy
Azithromycin	Fluconazole (3)	Increased risk of QT interval prolongation	Monitor ECG
	Ondansetron (2)	Increased risk of QT interval prolongation	Monitor ECG
Calcium acetate	Phenytoin (2)	Decreased exposure phenytoin	Consider separating the dose of oral phenytoin and antacids by several hours

Tab. No.24B: – Moderate Drug Interactions

Precipitant Drug	Interacting drug(No.)	Effect	Inference
Warfarin	Acetaminophen (3)	Increased risk of bleeding	Frequent monitoring of INR for several weeks when acetaminophen is added or discontinued
	Pantoprazole (4)	Increased INR ratio and prothrombin time	Warfarin dosage adjustments may be required
	Tramadol (4)	Increased risk of bleeding and prothrombin time	Monitor INR and adjust warfarin doses accordingly
Iron	Pantoprazole (4)	Reduced bioavailability	Monitor patient for iron efficacy if pantoprazole is being used concurrently
Atorvastatin	Clopidogrel (11)	High platelet reactivity	Discontinue statin
Torasemide	Clopidogrel (3)	Increased torasemide toxicity	Monitor torasemide toxicity
Calcium acetate	Levofloxacin (2)	Decreased levofloxacin effectiveness	Administer a different antibiotic or alternative therapy
Clobazam	Nebivolol (4)	Increased nebivolol plasma concentration	Dose reduction may be warranted for nebivolol
Metoprolol	Sitagliptin + metformin (3)	Results in hypoglycemia	Closely monitor for hypoglycaemia with concurrent use
Clobazam	Phenytoin (2)	Increased risk of phenytoin toxicity	Monitor for signs of phenytoin toxicity with combined therapy
Levothyroxine	Pantoprazole (3)	Increased TSH levels	Monitor TSH levels closely Adjust levothyroxine doses
Torasemide	Diclofenac (3)	Decreased diuretic and antihypertensive efficacy	Caution when NSAIDS and loop diuretics are co-administered
Calcium acetate	Ofloxacin (1)	Decreased ofloxacin effectiveness	Concurrent administration of ofloxacin and aluminium, calcium, or magnesium containing products is not recommended

Tab. No.24 C: - Minor Drug Interactions

Precipitant Drug	Interacting Drug(No.)	Effect	Inference
Calcium acetate	Iron (2)	Decreased iron effectiveness	It is not recommended else iron should be taken one hour before.
Calcium acetate	Atenolol (2)	Reduced effectiveness of atenolol	Atenolol should be administered two hours or six hours after the aluminum,calcium,magnesium containing product

STATATISTICAL ANALYSIS

The statistical analysis was done using SPSS software version 20. Chi square test had been used for the analysis. The statistical analysis had revealed the following results were an attempt to correlate the gender and risk scores obtained by using all the three scales revealed that there is a significant ($p < 0.05$)relationship between the risk score obtained and gender. Similarly, the risk scores were correlated with age of the study population which revealed a significant correlation.

The modifiable risk factors including presence of Diabetes mellitus, was found to be significant whereas the systemic hypertension and various stages of CKD didn't show any significance. The details were given in **Tab. No.25 -29**

Tab.No.25 A:- Chi square test risk scores Vs Gender

RISK ASSESSMENT		Gender		Total	p value
		Male, n(%)	Female, n(%)	n (%)	
Q-RISK ASSESSMENT	<10	0	0	0	0.052
	10-20	5(4.9)	9(8.8)	14(13.7)	
	21-30	17(16.7)	13(12.7)	30(29.4)	
	31-40	17(16.7)	13(12.7)	30(29.4)	
	≥40	22(21.6)	6(5.9)	28(27.5)	
WHO SCALE RISK ASSESSMENT	<10	1(0.9)	0	1(0.9)	0.017
	10-20	9(8.8)	13(12.7)	22(21.6)	
	21-30	15(14.7)	15(14.7)	30(29.4)	
	31-40	11(10.8)	8(7.8)	19(18.7)	
	≥40	25(24.7)	5(4.9)	30(29.4)	
FRAMINGHAMS RISK ASSESSMENTT	<10	0	0	0	0.007
	10-20	7(6.9)	9(8.8)	16(15.7)	
	21-30	14(13.7)	13(12.7)	27(26.5)	
	31-40	17(16.7)	16(15.7)	33(32.4)	
	≥40	23(22.6)	3(2.9)	26(25.4)	

Tab.No.26:- Chi square test risk score Vs Age

RISK ASSESSMENT		Age			Total	p value
		<70, n (%)	70-80, n(%)	>80, n(%)	n (%)	
Q-RISK ASSESSMENT	<10	0	0	0	0	0.001
	10-20	13(12.7)	1(0.9)	0	14(13.7)	
	21-30	21(20.6)	9(8.8)	0	30(29.4)	
	31-40	18(17.7)	11(10.9)	1(0.9)	30(29.4)	
	≥40	10(9.8)	11(10.9)	7(6.8)	28(27.5)	
WHO SCALE RISK ASSESSMENT	<10	1(0.9)	0	0	1(0.9)	0.161
	10-20	14(13.9)	7(6.8)	1(0.9)	22(21.6)	
	21-30	21(20.8)	8(7.8)	1(0.9)	30(29.4)	
	31-40	10(9.8)	9(8.9)	0	19(18.7)	
	≥40	16(15.8)	8(7.8)	6(5.9)	30(29.4)	
FRAMINGHAMS RISK ASSESSMENTT	<10	0	0	0	0	0.216
	10-20	12(11.8)	4(3.9)	0	16(15.6)	
	21-30	15(14.7)	11(10.9)	1(0.9)	27(26.5)	
	31-40	21(20.6)	10(9.8)	2(1.9)	33(32.4)	
	≥40	14(13.8)	7(6.8)	5(4.9)	26(25.5)	

Tab.No.27:- Chi square test risk scores Vs Diabetes Mellitus

RISK ASSESSMENT		Diabetes mellitus		Total	p value
		Yes, n (%)	No, n(%)	n (%)	
Q-RISK ASSESSMENT	<10	0	0	0	0.007
	10-20	4(3.9)	10(9.8)	14(13.7)	
	21-30	11(10.8)	19(18.6)	30(29.4)	
	31-40	13(12.7)	17(16.7)	30(29.4)	
	≥40	21(20.6)	7(6.9)	28(27.5)	
WHO SCALE RISK ASSESSMENT	<10	0	1(0.9)	1(0.9)	0.001
	10-20	4(3.8)	18(17.7)	22(21.6)	
	21-30	12(11.8)	18(17.7)	30(29.4)	
	31-40	11(10.9)	8(7.8)	19(18.7)	
	≥40	22(21.6)	8(7.8)	30(29.4)	
FRAMINGHAMS RISK ASSESSMENTT	<10	0	0	0	0.001
	10-20	3(2.9)	13(12.7)	16(15.7)	
	21-30	8(7.8)	19(18.6)	27(26.5)	
	31-40	21(20.6)	12(11.8)	33(32.3)	
	≥40	17(16.7)	9(8.9)	26(25.5)	

Tab.No.28:- Chi square test risk score Vs Hypertension

RISK ASSESSMENT		Hypertension		Total n (%)	p value
		Yes, n (%)	No, n(%)		
Q-RISK ASSESSMENT	<10	0	0	0	0.606
	10-20	7(6.9)	7(6.9)	14(13.7)	
	21-30	9(8.9)	21(20.6)	30(29.4)	
	31-40	11(10.9)	19(18.5)	30(29.4)	
	≥40	9(8.9)	19(18.5)	28(27.5)	
WHO SCALE RISK ASSESSMENT	<10	0	1(0.9)	1(0.9)	0.692
	10-20	9(8.9)	13(12.7)	22(21.7)	
	21-30	8(7.8)	22(21.6)	30(29.4)	
	31-40	8(7.8)	11(10.9)	19(18.6)	
	≥40	11(10.9)	19(18.5)	30(29.4)	
FRAMINGHAMS RISK ASSESSMENTT	<10	0	0	0	0.825
	10-20	7(6.9)	9(8.9)	16(15.7)	
	21-30	8(7.8)	19(18.6)	27(26.4)	
	31-40	12(11.8)	21(20.5)	33(32.4)	
	≥40	9(8.9)	17(16.6)	26(25.5)	

Tab.No.29:- Chi square test risk score Vs stages of kidney disease

RISK ASSESSMENT		Stage of kidney disease					Total n (%)	p value
		Stage 1, n (%)	Stage2, n(%)	Stage 3, n(%)	Stage 4,n(%)	Stage 5,n(%)		
Q-RISK ASSESSMENT	<10	0	0	0	0	0	0	0.133
	10-20	0	0	4(3.9)	4(3.9)	6(5.9)	14(13.7)	
	21-30	2(1.9)	1(0.9)	6(5.9)	10(9.8)	11(10.9)	30(29.4)	
	31-40	0	1(0.9)	7(6.9)	6(5.9)	16(15.7)	30(29.4)	
	≥40	0	3(2.9)	9(8.9)	12(11.8)	4(3.8)	28(27.5)	
WHO SCALE RISK ASSESSMENT	<10	0	0	0	1(0.9)	0	1(0.9)	0.609
	10-20	0	0	7(6.9)	7(6.9)	8(7.8)	22(21.7)	
	21-30	1(0.9)	1(0.9)	6(5.9)	8(7.8)	14(13.9)	30(29.4)	
	31-40	1(0.9)	1(0.9)	3(2.9)	5(4.9)	9(8.9)	19(18.6)	
	≥40	0	3(2.9)	10(9.8)	11(10.9)	6(5.9)	30(29.4)	
FRAMINGHAMS RISK ASSESSMENT	<10	0	0	0	0	0	0	0.144
	10-20	0	0	4(3.9)	7(6.9)	5(4.9)	16(15.7)	
	21-30	1(0.9)	0	7(6.9)	7(6.9)	12(11.8)	27(26.4)	
	31-40	0	1(0.9)	8(7.9)	8(7.9)	16(15.7)	33(32.4)	
	≥40	1(0.9)	4(3.9)	7(6.9)	10(9.8)	4(3.9)	26(25.5)	

8. DISCUSSION

Cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD) is high, and the presence of CKD worsens outcomes of cardiovascular disease (CVD). The study done by Nathan R .et al[11] on global prevalence of kidney disease was 13.4%. The current study shows a prevalence of 6.1 %. The study also revealed that male population is predominant and there were 59 males and 43 females among the study population. Various studies have mentioned about the predominance of male population for cardiovascular risk[11]. This study also shows that majority of study population's age was 65-74 years (new elderly old) and this category is more prone to cardiovascular disease and also studies report that age is another important non-modifying risk factor for CVD. Another modifiable risk factor is BMI and the assessment revealed that only 20% of the study population were found to be above the normal. The assessment on the smoking or use of tobacco revealed that the majority were found to be non-smokers and those were smoking were found in high risk category. The minimum length of stay in the hospital was found to 2 and when number of days of stay increases it may increase the cost of the treatment the patient. The average number of days of hospital stay was found to be 5.47 ± 2.64days. The assessment of reasons for admission to the study site revealed that majority patientswere admitted for breathing difficulty and swelling of limbs which were a classical symptom for CKD and also indicate a high risk to cardiovascular disease. The past medical and medication history of study population revealed that they were having diabetes mellitus and hypertension which are risk factors for diseases and the same is also which is cited in works done by Cláudia Bernardi et al.[27]

Family history of the patient having diabetes mellitus, systemic hypertension, chronic kidney disease are a non-modifying risk factor for CVD. The study report shows that 33% is having diabetes mellitus in their family history. The diagnosis of the study population also had revealed that majority of the population was having one or more modifying risk factors like Systemic Hypertension, Diabetes Mellitus and Chronic/Acute Kidney diseases. The present study also had variety of drugs prescribed respectively to the diseases condition of the study population and those drugs includes anti-hypertensives, proton pump inhibitors, diuretics, anti-lipidemic, anti-anginal, vitamin supplements, anti-epileptics, sedatives, anti-

inflammatory, antibiotics, etc. The average number of drugs prescribed was found to be8.009 ± 2.852. The maximum number of drugs given to patient is 14 and minimum is 3. The use of drugs to control the elevated condition which may pose a risk to cardiovascular system may reduce the risk of getting CVD. Various route of administration was preferred in geriatric patients. Oral route was the most preferred route of administration used for study population use followed by 83.33% injections drugs which may increase the cost of the treatment and also invites other complications associated with injectable and this may be because some cases non-availability of drugs likes aminoglycosides as oral dosage forms, patient comfort and rapid action. There was about 22.64% of total drug prescribed as injectable. In some situations switching from IV drugs to oral allow reduction in the hospital stay and potential benefits which reduces hospitalization costs and other related costs. The analysis of stages of CKD revealed that 48.03% patients were under stage III whereas the global prevalence of stage 3 was 7.6%[11].The very high prevalence in stage 3 patient may be because the patients were getting diagnosed and admitted to the hospital when the conditions were worsen and by the time patients were in stage 3 or stage 4. It was also found that the 30.39% were on haemodialysis because patients in stage 4 and stage 5 of CKD needs dialysis or kidney transplantation.

The prescription generated for the study population was analysed for any kind of drug related problems including drug dosage adjustments, medication error and ADR monitoring, drug-drug interactions, etc. The results revealed that only 2 incidence where drug dosage adjustment for renal insufficient patient was reported and .there was about 4 incidences where drug was prescribed without any indication and 4 incidences drug is required for indication. There were about 70 incidence of drug – drug interaction which account for 21 types of interactions including 6 major, 13 moderate and 2 minor interactions. The average number of drug-drug interactions was found to be 0.6568 ± 0.969

The risk assessment using WHO scale has revealed that females of the study population were found to be more in risk categories of 10-20% and 21-30% than their male counterparts. The assessment of the study population using QRISK calculators also revealed that females were predominant than males. The risk categories include 10-20%, 20-30% and 30-40%. A similar results was also obtained using Framingham's risk score calculator. The statistical analysis of the risk scores obtained were correlated with non-modifiable risk factors

like age and gender, modifiable factors like presence of diabetes mellitus, hypertension and stages of kidney disease has revealed a significant relationship in most of the cases. This category of very high risk will result in fatal or non-fatal vascular events and hence monitoring of risk factors are required for every 3-6 months. The rest of the population were male dominant in all the assessment. The monitoring of risk factors is required once in 6- 12 months and management with life style modifications. The patients were given counselling and appropriate interventions based on their risk category. The counselling/education given to the patient included life style modifications, diet modifications, awareness of intake of fats, salt, alcohol, fruits, vegetables, etc. Patients were also informed and made aware about reduction of BMI, weight, the target blood pressure, blood glucose levels, smoking cessation if the patient is smoker and about the importance's of being complaint to the physician's prescription like taking the prescribed drug for diabetes mellitus, systemic hypertension, lipid lowering or for chronic/acute renal failure.

If any individuals is at very high cardiovascular risk because they might had already experienced a cardiovascular event, or have very high levels of individual risk factors. Risk stratification is not necessary for making treatment decisions for these individuals, all of them need intensive lifestyle interventions and appropriate drug therapy. Risk prediction charts may tend to underestimate cardiovascular risk in such individuals, who include the following:

- Patients with established angina pectoris, coronary heart disease, myocardial infraction, ischemic attacks, stroke, peripheral vascular disease.
- Left ventricular hypertrophy or hypertensive retinopathy.
- Individuals without established CVD who have a cholesterol ≥8 mmol/l or LDL cholesterol ≥6mmol/l
- Individuals without established CVD who have persistent raised blood pressure(>160-170/100-105 mmHg)
- Patients with type 1 and type 2 diabetes, with over nephropathy or other significant renal disease.
- Patients with known renal failure or renal impairment.

9. PREVENTION OF CARDIOVASCULAR DISEASE

- Dietary change, weight control, avoidance of cigarettes and treatment of hypertension can favourably influence the risk profile of the elderly. Although no randomized controlled trials have been performed on modification of risk factors in the elderly except for hypertension, optimism as to likely efficacy is justified.

- Control of dyslipidemia, obesity and diabetes. Serum total and low density lipoprotein cholesterol can be lowered by decreased intake of cholesterol and saturated fat, with partial replacement of the saturated fat by polyunsaturated fat from vegetable and fish sources, by increased intake of water-soluble fiber and by reduction of overweight. Recent studies have shown a relation between the quantity and character of dietary fats, including fish oils, and coronary heart disease mortality. At least two recently completed controlled trials in younger populations have shown that reducing serum cholesterol by diet and drugs can lower coronary morbidity and mortality. The fat-modified diets required are nutritionally adequate, safe, convenient, inexpensive and palatable. Obesity aggravates all atherogenic traits in both young and old. Weight control with a well-balanced fat-modified diet is a major hygienic approach for improving all the atherogenic risk factors in young and old people. Preventive measures for the elderly diabetic at high risk for cardiovascular disease should include reduction of overweight; control of elevated blood pressure by dietary and, if needed, drug therapy; control of blood lipids and avoidance of cigarette smoking, in addition to control of blood sugar.

- Cigarette smoking. It is likely that smoking contributes to thrombotic occlusion and is a risk factor for occlusive peripheral arterial disease in the elderly. Cigarette smoking is also a major contributor to chronic bronchitis, emphysema and lung cancer in the elderly. Regular physical activity. This should be encouraged in the elderly because overall and cardiovascular mortality rates apparently are benefited at all ages, including the elderly.

- Control of hypertension. Hypertension is a major remediable risk factor for cardiovascular disease in the elderly because of its high prevalence and sustained impact in advanced age. Hypertension control should lessen the incidence of stroke, cardiac failure and renal insufficiency. Although the efficacy of correcting isolated systolic hypertension has not been demonstrated, its impact on risk in the elderly is established, early experience with its treatment is encouraging and a full-scale controlled trial is underway.

10. SUMMARY

The study entitled **"Assessment and Prevention of risk for development of Cardiovascular diseases in Geriatric population with Chronic kidney disease**" was carried out for a period of 10 months (December 2015 – September 2016). In this study, the data were collected from patients of the geriatric department of a private corporate tertiary care teaching hospital, during the ward rounds, as per the inclusion / exclusion criteria. The study carried out to assess the risk for cardiovascular events in patients with chronic kidney disease. The results obtained from the study may be summarized as follows:

- A total of 102 patients were enrolled in the study.
- The total number of patients admitted in hospital was found to be 1667 and 102 among were geriatric population with CKD who had been included in the study.
- The study results revealed that a predominant male population of 57.84% was observed among the study population.
- Age distribution of the study population was analyzed and it was found that 85.29% were in the age group 65-74 years in which males were 89.83% and females 79.06%
- The BMI results reveals that 79.40% were very well normal and do not have the risk
- It was found that 55.87% of study population had a stay of minimum 6 days in the hospital
- The analysis of reasons for admission to the study site had revealed that certain complaints like difficulty in breathing, vomiting, swelling of limbs, decreased urine output etc., were found to be very common
- Past medical history results revealed that diabetes mellitus, chronic renal failure and hypertension were very prevalent among the study population.
- The individual habit of taking of alcohol and tobacco becomes an important risk factor for most of clinical condition. In this regard 79.4%of study population didn't have the risk of having cardiovascular risk because they do not have the habit of smoking or drinking of alcohol.
- Laboratory investigation result had revealed that electrolytes serum creatinine, urea and GFR were commonly assessed to most of the study population as it have included CRF patients.

- Diagnosis results revealed that the modifying variable risk factors other than CRF, systemic hypertension, diabetes mellitus and renal failure were also very prevalent among the study population
- Drug categories analysis revealed that majority of the study population has received anti-hypertensive and antibiotics and proton pump inhibitors and almost majority of population has received one or more vitamin supplements. The average was found to be 8.009 ± 2.852. The maximum number of drugs given to patient is 14 and minimum is 3
- Route of administration result revealed that 83.33% of the drugs patients received were administrated as injections.
- The various stages of kidney disease is analysed and it was found that 48.03% population belongs to stage III.
- The analysis of drug-drug interactions prevailing in the prescriptions of study population had revealed that 44.11% of prescriptions were having one or more interaction and rest 55.88% didn't have even one drug-drug interaction. There were about 21 drug-drug interactions prevailing in the prescriptions of study population which account of a drug – drug interaction. The average was found to be 0.6568 ± 0.969
- QRISK scale had revealed that 29.41% of the study population were been categorised in the risk level of ≥40% in which 42.37% were males and 11.6% were females
- Framinghams risk score was found that 24.50% of population were at high risk in which males were 37.28% and females were 9.93%
- WHO charts results had revealed that 28.43% of the study population were been categorised in the risk level of ≥40% in which 33.89% were males and 4.65% were females. An overall 4.90% study population only were having risk of level less than 10%.

11. CONCLUSION

The study was carried out to assess the cardiovascular risk in geriatric patients, to provide prevention strategy for events in patients with chronic kidney disease, to assess the prescription patterns. The study concluded that there was an increased cardiovascular risk in geriatric patients with chronic kidney diseases. The study revealed that the male population in the study site were at greater risk and hypertension, diabetes mellitus as the major risk factor for cardiovascular disease. It was also concluded that use of QRISK calculator which do not require cholesterol assessment to calculate the cardiovascular risk can be made as a routine practice to assess and provide adequate prevention strategies of cardiovascular risk. Guidelines can be followed for the prevention and management of cardiovascular risk like by improving dietary intake, physical activity, weight control, life style advice etc. and also by providing awareness to the public by conducting health and nutrition education programs, and screening for early detection of cardiovascular disease. This study also revealed the importance of clinical pharmacist and their importance in providing pharmaceutical care to the patient for a better prognosis.

12. FUTURE OUTLOOK

The study may be extended to a large population and it shall be carried out to focus on safe and effective management of chronic kidney disease and cardiovascular risk in geriatric population, along with patient's awareness program which may be created and impact of the same may be also studied.

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DEPARTMENT OF PHARMACY PRACTICE
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Case No.: 3

TITLE: ASSESSMENT AND PREVENTION OF RISK FOR DEVELOPMENT OF CARDIOVASCULAR DISEASES IN GERIATRIC POPULATION WITH CHRONIC KIDNEY DISEASE

PATIENT DETAILS

Name	Age	Sex.	Wt.	Ht.	BMI	IP No.	Dept.	DOA	DOD
Mr. Velusamy	65	M	83	176	26.7	2016 01738	Gm	21/1	27/1

REASONS FOR ADMISSION C/O knee pain x 2 months

PAST MEDICAL HISTORY K/C/O CRF x 5yrs

PAST MEDICATION HISTORY –

FAMILY HISTORY –

SOCIAL HISTORY –

Known allergies: –

Tobacco in any form : Y / N Alcoholic : Y/N None : Y/N

Marital status : Married

LABORATORY INVESTIGATIONS

Date	D1	D2	D3	D4	D5	D6					Blood sugar (mg%)			
Temp.	N	N	N	N	N	N					F.B.S (60-90)			
BP	N	N	N	N	N	N					P.P.S(80-150)			
Pulse	N	N	N	N	N	N					R.B.S(90-110)			

BLOOD COUNTS

Haemoglobin (g/dl) M:12-16 F: 11-14	TLC (Cells/cumm) (5000-10000)	ESR (mm/hr) (M<10;F<20)	Differential Leukocyte Count (%)			
9.5	11,270	98	Polymorphs (40-60)			
			Lymphocytes (20-30)			
Platelets(1-3 lakhs)	Clotting Time(3-5 min)	Bleeding Time (1-3 min)	Basophils (0-1)			
4.1 38100			Eosinophils (1-4)			
			Monocytes (1-2)			

LIVER FUNCTION TEST

Total bilirubin (<1mg%)	0.4			Alk. Phosphatase (84-306 U/L)	268		
P.T. Time (14 Sec.)	16			SGPT (5-37 U/L)	13		

Bilirubin Direct : 0·2

Bilirubin Indirat : 0-20

Total protein : 6·5

Albumin : 3·5

Globulin 3·0

A/G ratio 1·20

SGOT 34

DEPARTMENT OF PHARMACY PRACTI

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Case No.:

MEDICATION CHART

S.No.	Name of the medication		Route	Dose(Per Day)	Frequency	Day of Treatment							
	Trade Name	Generic Name				D1	D2	D3	D4	D5	D6	D7	
01	Tab-Pan (b1F)	Pantoprazole	Oral	40mg	1-0-0								
02	T-Febuget	febxostat	Oral	80mg	0-0-1								
03	T-DOLO 6	Paracetamol	Oral	650mg	SOS	✓	✓	SOS	SOS	SOS	SOS	SOS	
04	Inj-Tramadol	Tramadol Hydrochl	IM	1amp	SOS	✓	✓	✓	✓	✓	✓	✓	
05	Inj-Rejuneron	Vitamin supplement	IV	1amp	OD	✓	✓	✓	✓	✓	✓	✓	
06	C-AOXITROL	Calcitrol		0.25mg	1-0-0	✓	✓	✓	✓	✓	✓	✓	
07	T-Lanum	calcium acetate			1-0-1	✓	✓	✓	✓	✓	✓	✓	
08	T-Awaytox	prc-Probiotro			1-0-1	✓	✓	✓	✓	✓	✓	✓	
09	T-Renosave	acetyl Cysteine/taurine			0-1-0	✓	✓	✓	✓	✓	✓	✓	
10	T-Lupred	Methyl prednisolone		4mg	1-0-0		✓	✓	✓	✓	✓	✓	
11	T-HCQS	Hydroxychloroquine Sulph		200mg	0-0-1		✓	✓	✓	✓	✓	✓	
12	T-Encefer D	Ferrous ascorbate folic		100mg	1-0-0		✓	✓	✓	✓	✓	✓	
13	T-Mebalet IR	Methylcobalamin		1500mg	1-0-0		✓	✓	✓	✓	✓	✓	
14													
15													
16													
17													
18													
19													
20													

DEPARTMENT OF PHARMACY PRACTICE
College of Pharmacy, SRIPMS, Coimbatore - 44
Email: pharmacy_practice@rediffmail.com Phone: 0422-4500297

Case No.:

TITLE: ASSESSMENT AND PREVENTION OF RISK FOR DEVELOPMENT OF CARDIOVASCULAR DISEASES IN GERIATRIC POPULATION WITH CHRONIC KIDNEY DISEASE

ELECTROLYTES (m.Eq/l)					**URINE EXAMINATION**	
Sodium (130-150)					Colour Pale yellow	Sugar NIL
Potassium (3.5-5.8)					Bile Salts -Ve	WBC
Chloride (98-100)					Bile Pigment -Ve	RBC
Bicarbonate(22-36)					Albumin Trace	Casts NIL
					Pus cells 2-3	Epithelial cells 1-2

RENAL FUNCTION TESTS														
Urea (mg%)(15-45)	88	68												
Uric acid (mg%) F-2-5, F-2-7	10.5	7.9												
eGFR	3.2	3.70	4	3.60	3.20	3.90	2.80							
Sr Creatinine (mg%) (0.6-1.4)	3.0	3.90	4	3.60	3.20	2.90	2.80							

Total Cholesterol			
LDL			
HDL			

Total Fluid Input(ml)	1200	2150	1400	2200	2500	1550	
Total Fluid output(ml)	700	1150	1900	2050	2600	1950	

Other Investigations :

DIAGNOSIS : CRF

RISK score = 22.2 %.

Discharge Medications:-

Tab pan 40mg 1-0-0 b/f x 7 days

T. Febuget 80mg 0-0-1 x 7 days

C. Aoxitrol 0.25mg 1-0-0 "

T. Lanum 1-0-1 "

T. Away fox 1-0-1 "

T. Renosave 0-1-0 "

T. Ivapred 4mg 1-0-0 "

T. Hcqs 200mg 0-0-1 "

T. encifer 0 0-1-0 "

T. nebala IR 1-0-0 "

T. Dolo 650mg 1-0-0 5 tabalets.

COLLEGE OF PHARMACY

Sri Ramakrishna Institute of Paramedical Sciences,
Coimbatore-44
Ph: 0422- 4500297, Email: pharmacy_practice@rediffmail .com

PATIENT INFORMATION FORM

Project Title: Assessment and prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease

I, **Jesni K Jose,**II year M.Pharm., (Pharmacy Practice)student of College of Pharmacy, SRIPMS, Coimbatore which is attached to Sri Ramakrishna Hospital Coimbatore, pursuinga dissertation work, entitled"**Assessment and prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease"**which has to be submitted to the Tamil Nadu Dr.M.G.R.MedicalUniversity, Chennai for partial fulfillment for the award of degree of Master of Pharmacy.The details about the patient and the treatment are required by the investigator for carrying out the dissertation. It is here by assured that the details collected are only for the purpose of research and it will helpful to the patient and care giver. It is also assured that the information obtained from the patient will be maintained confidentially. We hope you will provide us the necessary co-operation for the above mentioned work by providing a written consent.

Thanking you

Signature of the Supervisor

Dr.B. Rajalingam, M.Pharm, Ph.D.,
Assistant Professor,
Dept. of Pharmacy practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

Signature of the Investigator

Ms. Jesni K Jose,
II-M.Pharm,Pharmacy Practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

COLLEGE OF PHARMACY

Sri Ramakrishna Institute of Paramedical Sciences,
Coimbatore
Ph.: 0422- 4500297,
Email: pharmacy_practice@rediffmail.com

PATIENT CONSENT FORM

Project Title: Assessment and prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease

I Mr. VELUSAMY

have been made understood the necessity of the work entitled **"Assessment and prevention of risk for development of cardiovascular diseases in geriatric population with chronic kidney disease"** that is being carried out by **Ms. Jesni K Jose,** II year M.Pharm, (Pharmacy Practice) in College of Pharmacy, SRIPMS, Coimbatore. I voluntarily hereby agree by giving my consent to participate in this study and provide the necessary co-operation for the same.

Signature of the Patient/By-stander: Velusamy

Name of the Patient: VELUSAMY

Name of the By-stander: ப.வீரப்பன்

B. Rajalingam.
Signature of the Supervisor:

Dr. B. Rajalingam, M.Pharm, Ph.D.
Assistant Professor,
Dept. Of Pharmacy practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

Signature of the Investigators:

Ms. Jesni K Jose,
II M.Pharm,
Pharmacy Practice,
College of Pharmacy, SRIPMS,
Coimbatore-44

Place: Coimbatore

Date: 22/1/16

Sri Ramakrishna Hospital

Medical Service : M/s. S.N.R. SONS CHARITABLE TRUST

SRI RAMAKRISHNA HOSPITAL ETHICAL COMMITTEE

395, SAROJINI NAIDU ROAD, SIDHAPUDUR, COIMBATORE - 641 044.

Phone : 0422 - 4500000, 4500201, Grams :"RAMHOSP" Fax : 0422-2240521

E-mail : dean@snrsonstrust.org, website : sriramakrishnahospital.com

Ethics Committee Registration No. ECR/690/Inst/TN/2014

SRH/EC.5-7/2016-17

26th February 2016

ETHICAL CLEARANCE CERTIFICATE

Project title: "Assessment and Prevention of Risk for Development of Cardiovascular diseases in Geriatric Population with Chronic Kidney Disease".

Researcher: **Ms.Jesni K Jose**
M.Pharmacy II year,
Department of pharmacy Practice,
College of Pharmacy,
Sri Ramakrishna Institute of Paramedical Sciences,
Coimbatore – 641 044

The following members of the ethics committee were present at the meeting held on 20.02.2016 at 3.00pm at New Auditorium, Sri Ramakrishna Hospital Campus, Coimbatore.

SI NO	Members Name	Qualification	Designation	Address	Affiliation To the Institution Yes/NO
1.	Dr.P.Murali	M.Sc.,Ph.D., D.Sc	Scientist Mg. Director & CEO	Mg.Director & CEO Evolve Biotech Pvt.Ltd., 401 – 405, 4th floor Ticel Bio park Ltd, Taramani, Chennai - 13	No
2.	Dr.P.Sukumaran	MS., M.Ch., FIACS	Scientific / EC Member Secretary Dean	Dean Sri Ramakrishna Hospital, 395, Sarojini Naidu Road, Sidhapudur, Coimbatore	Yes
3.	Dr.T.Mohan Kumar	MD.,D.Sc., AB.,DPPR., FCCP.,	Clinician	Sr.Consultant Pulmonologist Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
4.	Dr.S.Rajagopal	M.Ch.,	Clinician	Sr. Consultant Neuro Surgeon Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes

Sri Ramakrishna Hospital

Medical Service : M/s. S.N.R. SONS CHARITABLE TRUST

SRI RAMAKRISHNA HOSPITAL ETHICAL COMMITTEE

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Ethics Committee Registration No. ECR/690/Inst/TN/2014

5.	Dr.R.Lalitha	DGO.,(OG)	Clinician	Sr.Consultant Gynecologist & HOD Sri Ramakrishna Hospital, 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
6.	Dr.T.K.Ravi	M.Pharm Ph.D	Scientific Member	Principal Sri Ramakrishna College of pharmacy 395, Sarojini naidu Road, Sidhapudur, Coimbatore.	Yes
7.	Dr.N.Paramasivan	MBBS.,MD	Basic Medical Scientist	Prof.of pharmacology and HOD Sri Ramakrishna Dental College and Hospital, Coimbatore.	Yes
8.	Dr.M.Rangasamy	B.E., M.Sc., Ph.D.,	Lay Person	Former Professor Government College of Technology, Coimbatore.	No

This is to certify that the research work entitled "Assessment and Prevention of Risk for Development of Cardiovascular diseases in Geriatric Population with Chronic Kidney Disease", placed before the Institutional Ethical Committee has been approved as there is no objection to do this research work.

This ethics committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

The Ethics Committee wishes her well in her research.

Yours Truly,

Member Secretary,
Institutional Human Ethics Committee,

Dr. P. SUKUMARAN, M.S.,M.Ch.,FIACS.,
Dean
SRI RAMAKRISHNA HOSPITAL,
395, Sarojini Naidu Road,
Sidhapudur, Coimbatore-641 044.

10-year CHD Risk Framingham Tables

Men

Estimate of 10-Year Risk for Men

(Framingham Point Scores)

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year Risk %
<0	< 1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥ 30

10-Year risk _____%

Women

Estimate of 10-Year Risk for Women

(Framingham Point Scores)

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year Risk %
< 9	< 1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥ 30

10-Year risk _____%

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health
National Heart, Lung, and Blood Institute

NIH Publication No. 01-3305
May 2001

WHO/ISH Risk prediction charts

for 14 WHO epidemiological sub-regions

1. Introduction

These charts indicate 10-year risk of a fatal or non-fatal major cardiovascular event (myocardial infarction or stroke), according to age, sex, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus for 14 WHO epidemiological sub-regions.

There are two sets of charts. One set can be used in settings where blood cholesterol can be measured. The other set is for settings in which blood cholesterol cannot be measured. Both sets are available according to the 14 WHO epidemiological sub-regions.

Each chart can only be used in countries of the specific WHO epidemiological sub-region, e.g. The charts for South East Asia sub-region B (SEAR B) can only be used in Indonesia, Sri Lanka and Thailand.

The list of WHO/ISH risk prediction charts by epidemiological sub-regions and the Member States in which they can be used are shown in table 1.

Table 1. List of WHO/ISH risk prediction charts by epidemiological sub-regions[1] and WHO Member States

WHO/ISH risk prediction charts by epidemiological sub-regions		WHO Member States
Africa	**AFR D**	Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome And Principe, Senegal, Seychelles, Sierra Leone, Togo
	AFR E	Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of The Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
The Americas	**AMR A**	Canada*, Cuba, United States of America*
	AMR B	Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts And Nevis, Saint Lucia, Saint Vincent and The Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela
	AMR D	Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru
Eastern Mediterranean	**EMR B**	Bahrain, Iran (Islamic Republic of), Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates
	EMR D	Afghanistan, Djibouti, Egypt, Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen
Europe*	**EUR A**	Andorra, Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom
	EUR B	Albania, Armenia, Azerbaijan, Bosnia And Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Poland, Romania, Serbia and Montenegro, Slovakia, Tajikistan, The Former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan
	EUR C	Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine
South-East Asia	**SEAR B**	Indonesia, Sri Lanka, Thailand
	SEAR D	Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, Nepal
Western Pacific	**WPR A**	Australia*, Brunei Darussalam, Japan, New Zealand*, Singapore
	WPR B	Cambodia, China, Cook Islands, Democratic People's Republic of Korea, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

[1] Mortality strata: A: very low child mortality and very low adult mortality; B: low child mortality and low adult mortality; C: low child mortality and high adult mortality; D: high child mortality and high adult mortality; E: high child mortality and very high adult mortality.

* Appropriate risk prediction charts already available

2. Instructions on how to use WHO/ISH (World Health Organization/International Society of hypertension) risk prediction charts

The charts provide approximate estimates of cardiovascular disease (CVD) risk in people who do not have established coronary heart disease, stroke or other atherosclerotic disease. They are useful as tools to help identify those at high cardiovascular risk, and to motivate patients, particularly to change behaviour and, when appropriate, to take antihypertensive, lipid-lowering drugs and aspirin.

How do you use the charts to assess cardiovascular risk?

- First make sure that you select the appropriate charts using information in table 1
- If blood cholesterol cannot be measured due to resource limitations, use the charts that do not have total cholesterol
- Before applying the chart to estimate the 10-year cardiovascular risk of an individual, the following information is necessary
  - Presence or absence of diabetes[1]
  - Gender
  - Smoker or non-smoker
  - Age
  - Systolic blood pressure[2]
  - Total blood cholesterol (if in mg/dl divide by 38 to convert to mmol/l)

Once the above information is available proceed to estimate the 10-years cardiovascular risk as follows.

Step 1 Select the appropriate chart depending on the presence or absence of diabetes[1]

Step 2 Select male or female tables

Step 3 Select smoker or non smoker boxes[3]

Step 4 Select age group box (if age is 50-59 years select 50, if 60-69 years select 60 etc)

Step 5 Within this box find the nearest cell where the individuals systolic blood pressure (mm Hg) and total blood cholesterol level (mmol/l)[4] cross. The colour of this cell determines the 10-year cardiovascular risk.

---

1. A person who has diabetes is defined as someone taking insulin or oral hypoglycaemic drugs, or with a fasting plasma glucose concentration above 7.0 mmol/l (126 mg/dl) or a postprandial (approximately 2 hours after a main meal) plasma glucose concentration above 11.0 mmol/l (200 mg/l)on two separate occasions). For very low resource settings urine sugar test may be used to screen for diabetes if blood glucose assay is not feasible. If urine sugar test is positive a confirmatory blood glucose test need to be arranged to diagnose diabetes mellitus.
2. Systolic blood pressure, taken as the mean of two readings on each of two occasions, is sufficient for assessing risk but not for establishing a pretreatment baseline.
3. All current smokers and those who quit smoking less than 1 year before the assessment are considered smokers for assessing cardiovascular risk.
4. The mean of two non-fasting measurements of serum cholesterol by dry chemistry, or one non-fasting laboratory measurement, is sufficient for assessing risk.

Practice points

Please note that CVD risk may be higher than indicated by the charts in the presence of the following:

- already on antihypertensive therapy
- premature menopause
- approaching the next age category or systolic blood pressure category
- obesity (including central obesity);
- sedentary lifestyle;
- family history of premature coronary heart disease (CHD) or stroke in first degree relative (male < 55 years, female < 65 years);
- raised triglyceride level (>2.0 mmol/l or 180 mg/dl);
- low HDL (high density lipoprotein) cholesterol level (< 1 mmol/l or 40mg/dl in males, < 1.3 mmol/l or 50 mg/dl in females);
- raised levels of C-reactive protein, fibrinogen, homocysteine, apolipoprotein B or Lp(a), or fasting glycaemia, or impaired glucose tolerance;
- microalbuminuria (increases the 5-year risk of diabetics by about 5%) (38, 83, 85);
- raised pulse rate.
- socioeconomic deprivation

Risk levels

The colour of the cell indicates the 10-year risk of combined myocardial infarction and stroke risk (fatal and non-fatal) as shown below.

10-year combined myocardial infarction and stroke risk (fatal and non-fatal)

	Green	<10%
	Yellow	10% to <20%
	Orange	20% to <30%
	Red	30% to <40%
	Deep Red	≥ 40%

7. South East Asia

WHO sub-regions SEAR B, SEAR D

Charts in colour for use in settings where total blood cholesterol can be measured

Figure 21. WHO/ISH risk prediction chart for SEAR B

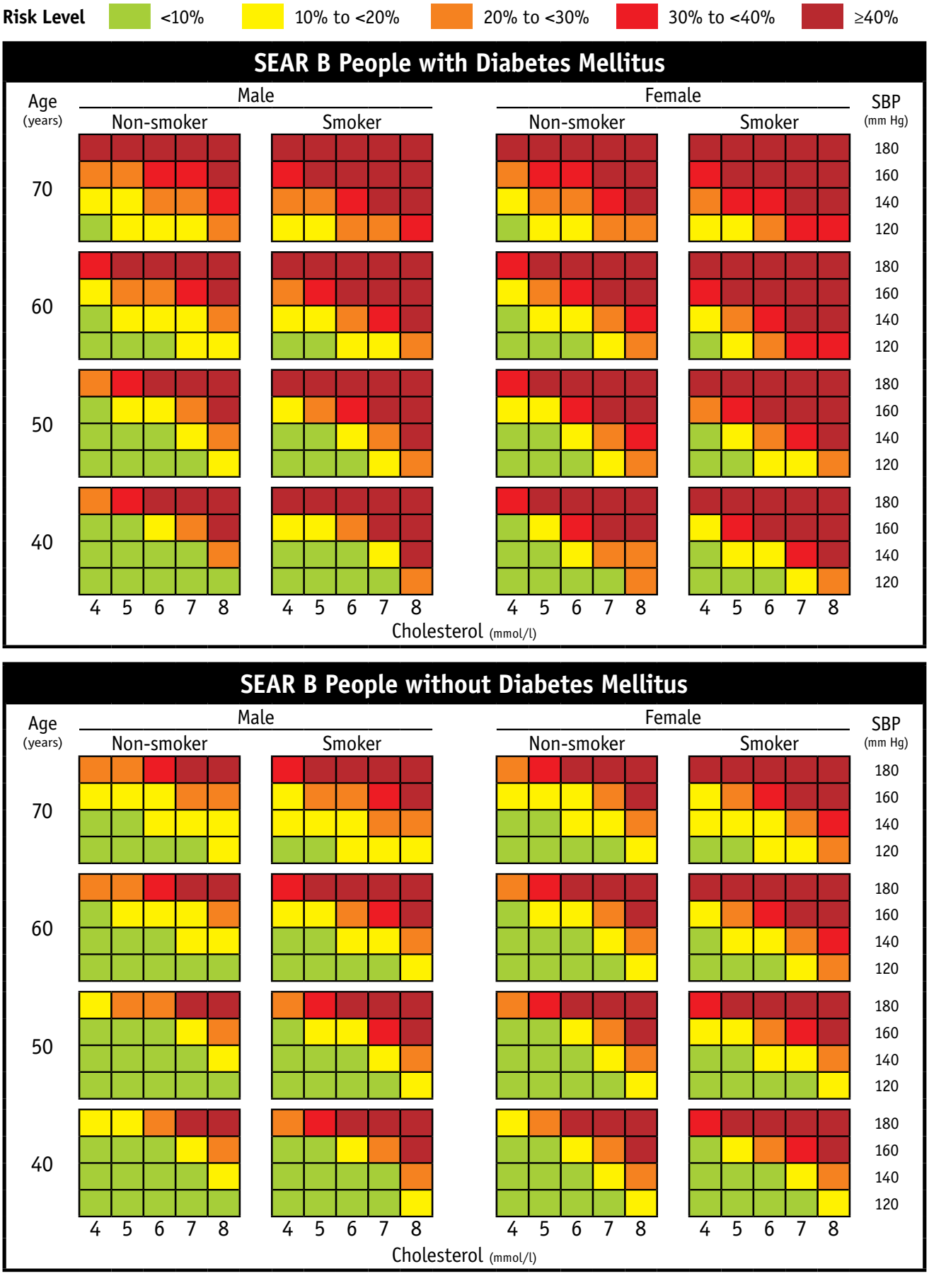
Figure 22. WHO/ISH risk prediction chart for SEAR D

Charts in colour for use in settings where total blood cholesterol cannot be measured

Figure 23. WHO/ISH risk prediction chart for SEAR B

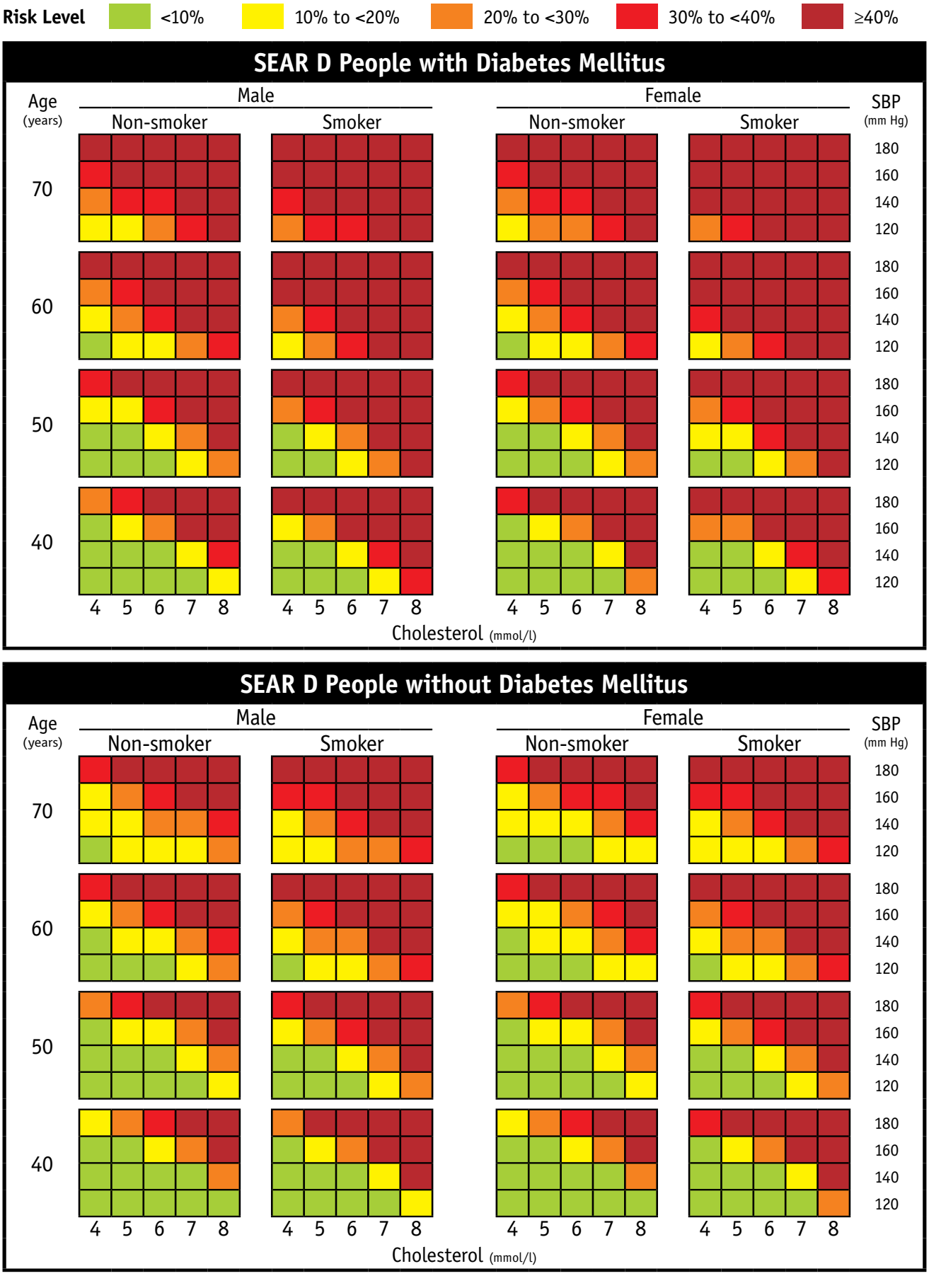
Figure 24. WHO/ISH risk prediction chart for SEAR D

Figure 21. WHO/ISH risk prediction chart for SEAR B. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus.



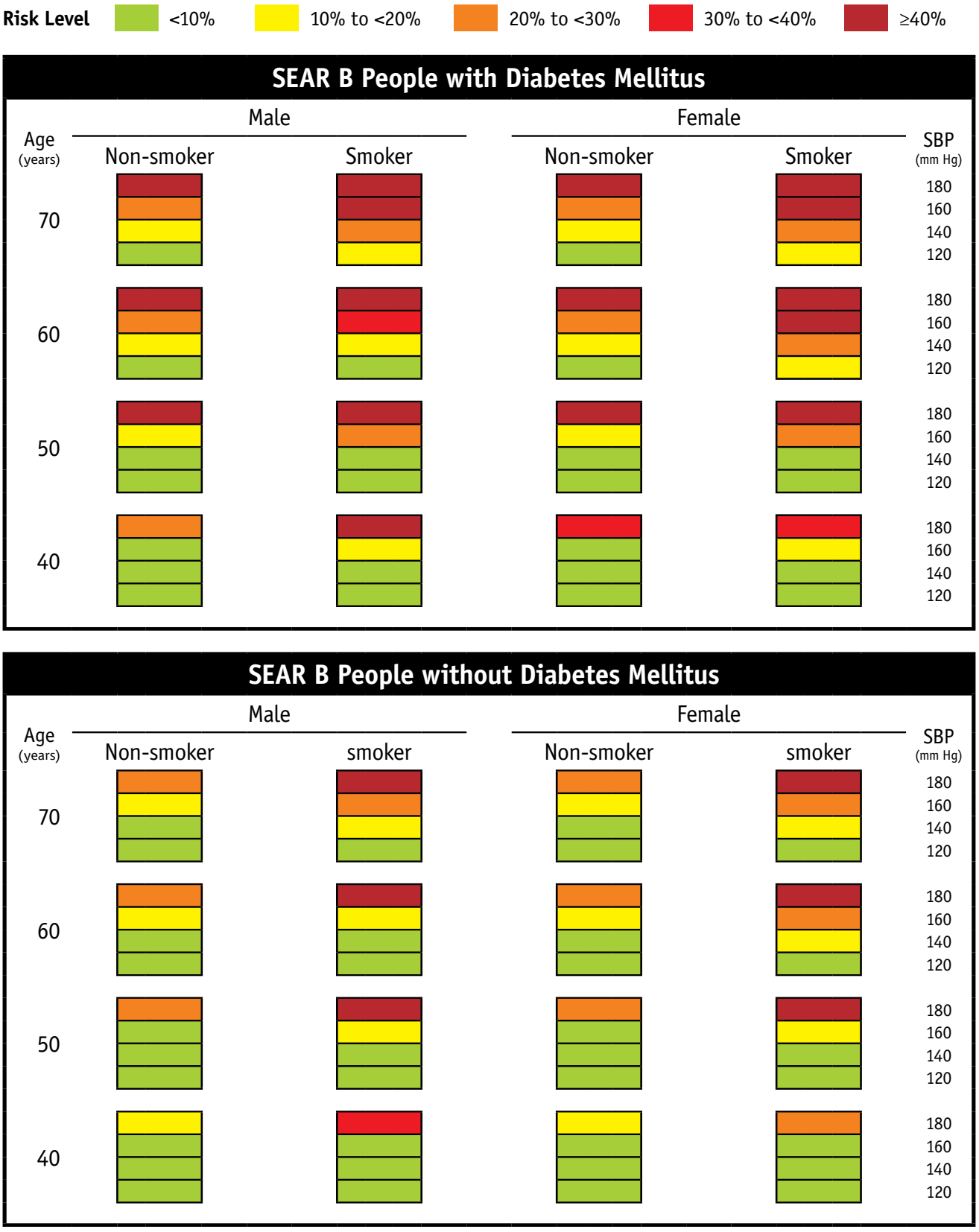
This chart can only be used for countries of the WHO Region of South-East Asia, sub-region B, in settings where blood cholesterol can be measured. (see Table 1)

Figure 22. WHO/ISH risk prediction chart for SEAR D. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus.



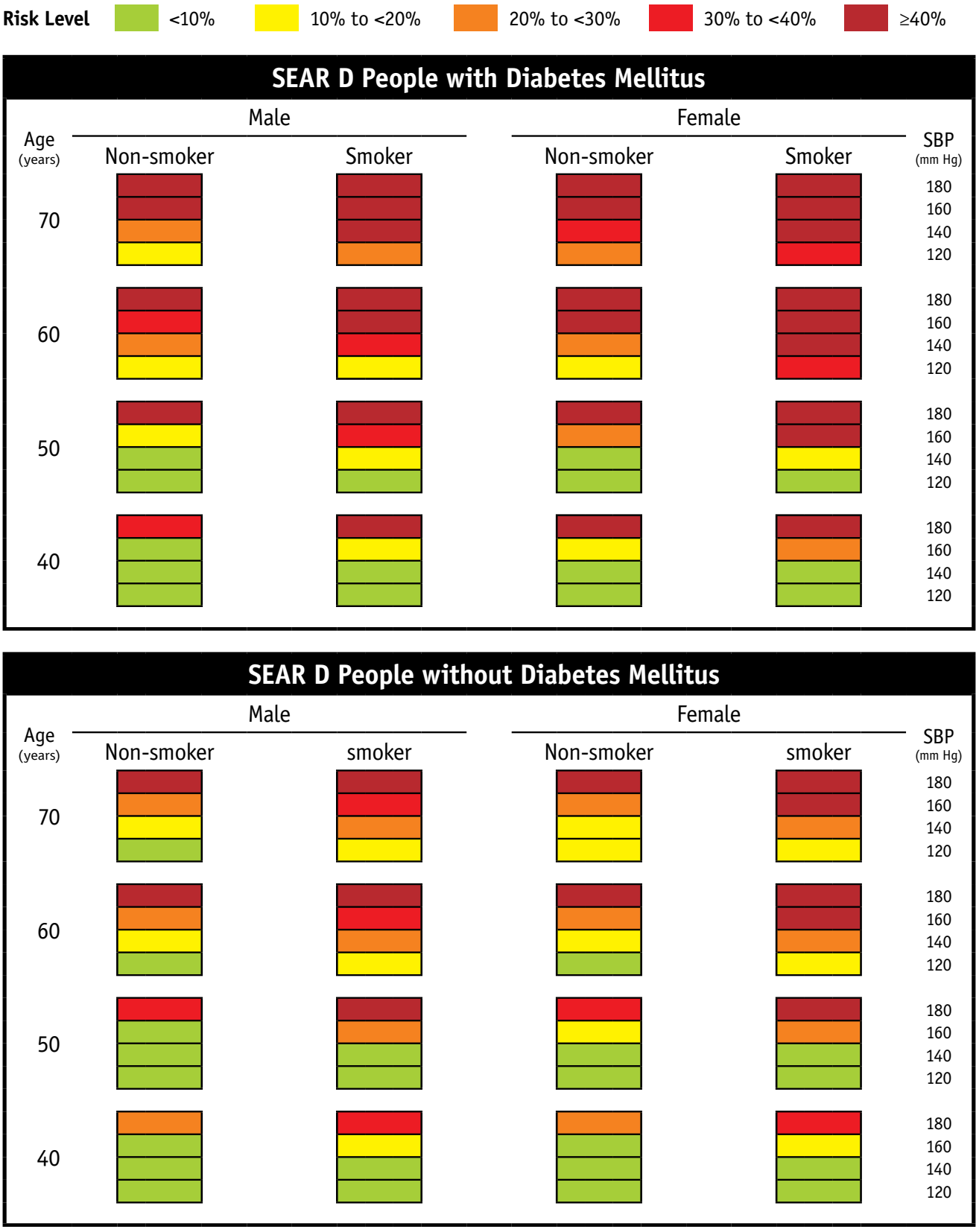
This chart can only be used for countries of the WHO Region of South-East Asia, sub-region D, in settings where blood cholesterol can be measured (see Table 1).

Figure 23. WHO/ISH risk prediction chart for SEAR B. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus.



This chart can only be used for countries of the WHO Region of South-East Asia, sub-region B, in settings where blood cholesterol CANNOT be measured (see Table 1).

Figure 24. WHO/ISH risk prediction chart for SEAR D. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus.



This chart can only be used for countries of the WHO Region of South-East Asia, sub-region D, in settings where blood cholesterol CANNOT be measured. (see Table 1)