Prevalence of Cardiovascular Disease in Patients with Chronic Kidney Disease in Some Hospitals of Dhaka.

A thesis report submitted to the department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the requirements for the degree of M. Pharm in Clinical Pharmacy and Molecular Pharmacology

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Declaration by the Research Candidate

I, Md. Nayem Islam Khan, hereby declare that the dissertation entitled "Prevalence of Cardiovascular Disease In patients with Chronic Kidney Disease in Some Hospitals of Dhaka", submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree of M. Pharm in Clinical Pharmacy and Molecular Pharmacology (Masters) is a bona fide record of original research work carried out by me under the supervision and guidance Farhana Rizwan , Assistant Professor, Dept. of Pharmacy, East West University and it has not formed the basis for the award of any other Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Place: Dhaka

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Certificate

This is to certify that the thesis "Prevalence of Cardiovascular Disease In patients with Chronic Kidney Disease in Some Hospitals of Dhaka", submitted to the department of pharmacy, East West University in partial fulfillment of the requirements of the degree of M. Pharm in Clinical Pharmacy and Molecular Pharmacology was carried out by Md. Nayem Islam Khan (ID# 2013-3-79-018) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information and laboratory facilities availed of in this connection is duly acknowledged.

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Certificate

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Abstract

The present study was designed to investigate the prevalence of cardiovascular disease in patients with chronic kidney disease in some hospitals of Dhaka. One hundred and seventy two respondents were selected by purposive sampling method as samples for the present study. The main objective of the present study was to investigate the presence of cardiovascular disease in chronic kidney disease patients. The specific objectives were: (i) To investigate prevalence of cardiovascular disease in chronic kidney disease patients, (ii) To investigate how much CKD patients have cardiovascular disease or risk of cardiovascular disease. For collecting data physical health questionnaires were applied on the respondents of the present research. And we found that prevalence of Atherosclerotic Heart Disease (ASHD) in CKD patients was 41.28% and subsequently Acute Myocardial Infarction (AMI) in CKD patients was 11.05% Congestive Heart Failure (CHF) in CKD patients was 27.33%, Peripheral Artery Disease (PAD) in CKD patients was 25.58%. Prevalence of CVD in patients with CKD in Bangladesh is very high. Presence of CKD appears to be an independent risk factor for CVD outcomes, particularly in higher-risk populations. Beside those, patients with CKD should be considered in the highest-risk group for CVD events.

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Chapter One - Introduction

1. Introduction

Chronic Kidney disease is one of the most devastating risk factor of cardiovascular diseases. Although it is individually life threatening, disease situations become worsen when it associates with cardiovascular disease. In result mortality rate is becoming very higher in patients with CKD which also have CVD. So, globally it has become very important area of concern for the healthcare providers as well as patients.

1.1 Chronic kidney disease:

Chronic kidney disease, also called chronic kidney failure, describes the gradual loss of kidney function. Kidneys filter wastes and excess fluids from your blood, which are then excreted in your urine. When chronic kidney disease reaches an advanced stage, dangerous levels of fluid, electrolytes and wastes can build up in your body.

In the early stages of chronic kidney disease have few signs or symptoms. Chronic kidney disease may not become apparent until kidney function is significantly impaired.

Treatment for chronic kidney disease focuses on slowing the progression of the kidney damage, usually by controlling the underlying cause. Chronic kidney disease can progress to end-stage kidney failure, which is fatal without artificial filtering (dialysis) or a kidney transplant.

1.2 Pathophysiology of Chronic kidney disease:

Pathophysiologic changes within the kidney depend on the etiology of CKD. When an individual has a diagnosis of CKD there is nephron dysfunction that persists three months or longer resulting in irreversible kidney damage. These dysfunctional changes to the kidney impair glomerular function and predispose the remaining viable nephron to sclerosis (pathological hardening of the tissue).

Azotemia (retention of nitrogenous waste products) occurs as CKD develops. Other pathophysiological changes include uremia, fluid retention, and excessive weight gain. Uremia consists of an accumulation of products that affect protein metabolism, and loss of kidney function that results in fluid and electrolyte imbalances. Common symptoms of uremia include nausea, vomiting, fatigue, anorexia, weight loss, muscle cramps, and change in mental status (Counts et al., 2008). Uremia often leads to major disturbances in the function of all other body systems such as a decline in endocrine abnormalities due to high level of toxicity, cardiovascular abnormalities from left ventricular hypertrophy, and gastrointestinal disturbances from malnutrition (Miller, 2015).

1.3 Types of Chronic Kidney Disease:

a. Chronic Pre-Renal Kidney Failure: When low blood flow to the kidneys is not treated and the condition remains for an extended period of time, chronic pre-renal kidney failure can occur. The kidneys begin to shrink and lose the ability to function.

b. Chronic Intrinsic Kidney Failure: Damage to the kidneys over an extended period due to intrinsic kidney disease can develop into chronic intrinsic kidney failure.

c. Chronic Post-Renal Kidney Failure: This happens when a long-term blockage of the urinary tract prevents urinary waste elimination, which causes pressure and eventual kidney damage (Smeltzer et al., 2010).

1.4 Stages of Chronic Kidney Disease:

The National Kidney Foundation set 5 chronic kidney failure stages to determine the severity of the disease. The chronic kidney failure stages are based on the GFR level (glomerular filtration rate), which is a measurement of how quickly your kidneys are able to clean your blood.

If kidneys are healthy and functioning normally, GFR level will be 90 mL/min or greater.
Stages Normal = Healthy Kidneys with a GFR level of 90 mL/min or greater
Stage 1 = Kidney damage but normal or high GFR of 90 mL/min or greater
Stage 2 = mildly decreased GFR of 60 to 89 mL/min
Stage 3 = moderately decreased GFR of 30 to 59 mL/min
Stage 4 = severely decreased GFR of 15 to 29 mL/min
Stage 5 = Kidney failure or dialysis. GFR of Less than 15 mL/min (Perneger, 1994).

1.4.1 Stage 1 & Stage 2

In stages 1 and 2, there may be no noticeable symptoms. In these chronic kidney failure stages, the disease is usually diagnosed through lab tests that detect associated conditions such as high blood pressure, higher than normal levels of creatinine or urea in the blood, blood or protein in the urine, or evidence of kidney damage (i.e. MRI, CT scan, Ultrasound, contrast X-ray) (Perneger, 1994).

1.4.2 Stage 3

A person with stage 3 chronic kidney disease (CKD) has moderate kidney damage. This stage is broken up into two: a decrease in glomerular filtration rate (GFR) for Stage 3A is 45-59 mL/min and a decrease in GFR for Stage 3B is 30-44 mL/min. As kidney function declines waste products can build up in the blood causing a condition known as “uraemia.” In stage 3 a person is more likely to develop complications of kidney disease such as high blood pressure, anaemia (a shortage of red blood cells) and/ or early bone disease (Perneger, 1994).

1.4.3 Stage 4

In stage 4, kidneys are losing the ability to properly remove waste products and excess water from body and need to prepare for dialysis treatments or a kidney transplant (Perneger, 1994).

1.4.4 Stage 5:

Stage 5, is also called end stage kidney disease, or end stage renal disease (ESRD). In this stage there is a complete or near complete loss of kidney function. Body accumulates wastes, water, and toxic substances because the kidneys are unable to clear them from the body. In this stage, need dialysis or a kidney transplant to survive. Acute kidney problems can be caused by infection, injury, certain medical conditions, and certain medications (Perneger, 1994).

1.5 Cardiovascular diseases:

Cardiovascular diseases are a group of disorders of the heart and blood vessels and including- coronary heart disease, cerebrovascular disease, peripheral arterial, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism.

1.6 Global impact of cardiovascular diseases:

CVDs are the number 1 cause of death globally. An estimated 17.5 million people died from CVDs in 2012, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. Over three quarters of CVD deaths take place in low- and middle-income countries. Out of the 16 million deaths under the age of 70 due to noncommunicable diseases, 82% are in low and middle income countries and 37% are caused by CVDs.

1.7 Types of cardiovascular disease:

- **Coronary heart disease –** Coronary heart disease (CHD) is a narrowing of the small blood vessels that supply blood and oxygen to the heart. CHD is also called coronary artery disease. Coronary heart disease is caused by the buildup of plaque in the arteries to your heart. This may also be called hardening of the arteries. Fatty material and other substances form a plaque buildup on the walls of your coronary arteries. The coronary arteries bring blood and oxygen to your heart. This buildup causes the arteries to get narrow. As a result, blood flow to the heart can slow down or stop.
- **Cerebrovascular disease –**Cerebrovascular disease refers to a group of conditions that affect the circulation of blood to the brain, causing limited or no blood flow to affected areas of the brain. Atherosclerosis is one of the conditions that can cause cerebrovascular disease. During this process, high cholesterol levels coupled with inflammation in areas of the arteries in the brain can cause the cholesterol to build up in the vessel in the form of a thick, waxy plaque. This plaque can limit, or completely obstruct, blood flow to the brain, causing a stroke,

transient ischemic attacks, or dementia, which may lead to a variety of other health complications. The most common forms of cerebrovascular disease are cerebral thrombosis (40% of cases) and cerebral embolism (30%), followed by cerebral hemorrhage (20%).

- **Peripheral arterial disease** – Peripheral artery disease (P.A.D.) is a disease in which plaque builds up in the arteries that carry blood to your head, organs, and limbs. Plaque is made up of fat, cholesterol, calcium, fibrous tissue, and other substances in the blood. When plaque builds up in the body's arteries, the condition is called atherosclerosis. Over time, plaque can harden and narrow the arteries. This limits the flow of oxygen-rich blood to your organs and other parts of your body. PAD usually affects the arteries in the legs, but it also can affect the arteries that carry blood from your heart to your head, arms, kidneys, and stomach. This article focuses on P.A.D. that affects blood flow to the legs.

- **Rheumatic heart disease** – Damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria. Rheumatic heart disease describes a group of short-term (acute) and long-term (chronic) heart disorders that can occur as a result of rheumatic fever. One common result of rheumatic fever is heart valve damage. This damage to the heart valves may lead to a valve disorder.

- **Congenital heart disease –** Malformations of heart structure existing at birth. Congenital heart defects are problems with the heart's structure that are present at birth. Congenital heart defects change the normal flow of blood through the heart. Congenital heart defects are the most common type of birth defect, affecting 8 out of every 1,000 newborns. There are many types of congenital heart defects ranging from simple to very complex. Although many heart defects have few or no symptoms, some do. Severe defects can cause symptoms such as: Rapid breathing, a bluish tint to skin, lips, and fingernails, fatigue (tiredness), poor blood circulation. Serious heart defects are usually diagnosed while a baby is still in the womb or soon after birth. Some defects aren't diagnosed until later in childhood, or even in adulthood.

- **Deep vein thrombosis and pulmonary embolism** – Deep vein thrombosis (throm-BO-sis), or DVT, is a blood clot that forms in a vein deep in the body. Blood clots occur when blood thickens and clumps together. Most deep vein blood clots occur in the lower leg or thigh. They also can occur in other parts of the body. A blood clot in a deep vein can break off and travel through the bloodstream. The loose clot is called an embolus. It can travel to an artery in the lungs and block blood flow. This condition is called pulmonary embolism or PE.

- **Acute myocardial infarction (AMI)-** Commonly known as a heart attack, occurs when blood flow stops to a part of the heart causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck, or jaw.

Often it is in the center or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat, or feeling tired.

- **Congestive heart failure-** Congestive heart failure (CHF) is a chronic progressive condition that affects the pumping power of heart muscles. While often referred to simply as "heart failure," CHF specifically refers to the stage in which fluid builds up around the heart and causes it to pump inefficiently. CHF develops when your ventricles can't pump blood in sufficient volume to the body.

Heart attacks and strokes are usually acute events and are mainly caused by a blockage that prevents blood from flowing to the heart or brain. The most common reason for this is a build-up of fatty deposits on the inner walls of the blood vessels that supply the heart or brain. Strokes can also be caused by bleeding from a blood vessel in the brain or from blood clots. The cause of heart attacks and strokes are usually the presence of a combination of risk factors, such as tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol, hypertension, diabetes and hyperlipidaemia.

1.8 Risk factors of cardiovascular disease:

There are a number of risk factors for CVD, including:

- High blood pressure (hypertension)
- Smoking
- High blood cholesterol
- Diabetes
- Lack of exercise
- Being overweight or obese
- A family history of heart disease
- Ethnic background etc.

1.9 Risk Factors for CVD in CKD:

Established 'traditional' atherosclerotic risk factors, such as diabetes, hypertension, dyslipidemia, and older age, have been found to be independent predictors of CVD in CKD. In addition, hemodynamic and metabolic factors such as volume overload, anemia, calcium and phosphorus imbalance, chronic insuffrioiciency that may contribute to the risk and pathogenesis of CVD. In renal transplant patients factors such as source of donation, graft failure, and type of immunosuppressive therapy may play a role. Several of the traditional risk factors in the general population demonstrate a phenomenon known as 'reverse epidemiology' in the CKD population. For example, obesity and hypertension are established CVD risk factors in the general population, whereas lower body mass index and hypotension have been shown to be risk factors for cardiovascular mortality in ESRD. To date, there has only been one prospective observational study of dialysis patients that controlled for baseline cardiac function. (Foley et al.).

They found that a 10 mm Hg mean blood pressure increase was associated with a 44% higher risk of developing CHF and that patients with chronic CHF or LVH are at higher risk of mortality compared with patients without these cardiac abnormalities.

Chapter Two -

Literature Review

2. 1 Cardiovascular Disease in Patients with CKD:

Cardiovascular disease remains the leading cause of death in most developed countries including the United States and accounts for over half the deaths among those on dialysis. Death from cardiovascular disease is far more common in patients with chronic kidney disease (CKD) than progression to end-stage renal disease (ESRD) (Gargiulo et al., 2015). CKD has been recognized as an independent risk factor for cardiovascular disease and has now been recognized as a coronary disease risk equivalent (Briasoulis and Bakris, 2013), similar to diabetes mellitus. The complex relationship between cardiovascular disease and kidney disease is thought to be due to shared traditional risk factors (e.g., diabetes mellitus, hypertension, physical inactivity, left ventricular hypertrophy, smoking, family history, and dyslipidemia), as well as the influence of non-traditional risk factors in the presence of CKD (e.g., endothelial dysfunction, vascular medial hyperplasia, sclerosis and calcification, volume overload, abnormalities in mineral metabolism, anemia, malnutrition, inflammation, oxidative stress, and autonomic imbalance). The cardio-renal syndrome continues to pose both a diagnostic and therapeutic challenge for those with heart failure (Husain-Syed et al., 2015). Not surprisingly, cardiovascular disease is often an important comorbidity among patients with CKD.

2.2 High prevalence of chronic kidney disease in a community survey of urban Bangladeshis:

The burden of chronic kidney disease (CKD) will rise in parallel with the growing prevalence of type two diabetes mellitus in South Asia but is understudied. Using a cross-sectional survey of adults living in a middle income neighborhood of Dhaka, Bangladesh, we tested the hypothesis that the prevalence of CKD in this group would approach that of the U.S. and would be strongly associated with insulin resistance. We enrolled 402 eligible adults (>30 years old) after performing a multi-stage random selection procedure. We administered a questionnaire, and collected fasting serum samples and urine samples. We used the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to estimate glomerular filtration rate, and sex-specific cut offs for albuminuria: > 1.9 mg/mmol (17 mg/g) for men, and >2. 8 mg/mmol (25 mg/g) for women. We assessed health-related quality of life using the Medical Outcomes Study Short Form-12 (SF-12).Results: A total of 357 (89%) participants with serum samples comprised the analytic cohort. Mean age of was 49.5 (± 12. 7) years. Chronic kidney disease was evident in 94 (26%). Of the participants with CKD, 58 (62%) had albuminuria only. A participant with insulin resistance had a 3.6-fold increase in odds of CKD (95% confidence interval 2.1 to 6.4). Participants with stage three or more advanced CKD reported a decrement in the Physical Health Composite score of the SF-12, compared with participants without CKD We found an alarmingly high prevalence of CKD particularly CKD associated with insulin Resistance in middle-income, urban Bangladeshis (Anand et al. 2009).

2.3 Prevalence of Cardiovascular Disease In patients with Chronic Kidney Disease in USA:

The prevalence of cardiovascular disease in USA is 69.6% among patients aged 66 and older who have CKD, compared to 34.7% among those who do not have CKD. The presence of CKD worsens the short- and long-term prognosis for many common cardiovascular diseases. The two-year survival of AMI patients without a diagnosis of CKD is 57%, compared to 46% for CKD Stage 1-2 patients and 30% for CKD Stage 4-5 patients. Over a two-year period, Medicare patients with both congestive heart failure and CKD have an adjusted survival probability of 75.3%, compared with 88.9% for those with CKD alone. Atrial fibrillation is common among Medicare patients with CKD (24.1%). The prevalence of atrial fibrillation rises for males with more advanced stages of CKD, age, hypertension, and congestive heart failure. Nearly half of CKD patients with congestive heart failure have a diagnosis of atrial fibrillation.

2.4 Prevalence of Cardiovascular Disease In patients with Chronic Kidney Disease in Nepal:

Patients with CKD are more likely to die of CVD than to develop kidney failure6. The alarming rise in CKD appears not to be due to intrinsic renal disease but to the dramatic rise in systemic diseases that damage the kidney. These include type 2 diabetes and atherosclerotic disease. Patients with CKD have an increased risk for major cardiovascular morbidity and mortality. Such increased cardiovascular risk begins quite early in renal insufficiency4. CKD and CVD share a number of common aetiological factors. Moreover the circumstances derived from disease in one system can negatively influence the other organ system10. But even after adjusting for such factors, the association of CKD with prevalence of cardiovascular disease is seen to persist. This prompted the American Heart Association in 1993 to recommend that patients with CKD be considered members of the “highest risk group” for development of subsequent cardiovascular events. As CVD in CKD is treatable and potentially preventable, assessment of major risk factors prevalent in resource poor settings like ours becomes important. We found a higher prevalence of diabetes mellitus in the CKD group as compared to the control population (OR = 1.67). Truncal obesity as well as deranged lipid profile was higher among CKD group in both the sexes than the control group. It is important to realise that these factors are treatable and potentially preventable, mostly with simple lifestyle modifications. Measures like physical exercise, dietary modification and smoking cessation could potentially have highly favourable outcomes and minimise the CVD risk factors. Among those cases 54.8% had a sedentary lifestyle whereas smokers were also higher among cases (OR = 3.67). Awareness, health promotion and lifestyle modification seem to be the most effective and economically sound interventions to control these factors in developing countries. Findings show a higher prevalence of hypertension in the cases than the controls (OR = 2.16). Early detection and institution of anti-hypertensive therapy is the key factor. This has been specifically stressed by Joint National Committee (JNC-7) which includes CKD as a “compelling” indication, justifying lower target blood pressure and treatment with specific anti-hypertensive agents. Anaemia (haemoglobin < 12 g/dl) was observed in 55.2% of cases compared to 21.1% of the controls (OR = 4.0). This uraemia-related risk factor shares a close relationship between cardiovascular morbidity and mortality14. Data from Medicare considered anaemia a multiplicative risk factor for mortality in patients with CKD. It

is also associated with causation of cardiomyopathy. Proteinuria, reduced GFR and creatinine clearance are other independent risk factors for development of CVD (Sarathi Kalra, 2009).

2.5 Epidemiology and prevention of cardiovascular complication in chronic kidney disease patients:

CKD patients are exposed to a number of cardiovascular risk factors, also including the so-called traditional ones, which are observed with particular frequency among patients with CKD compared with the general population. Indeed, it has been shown that the prevalence of all of the major traditional cardiovascular risk factors other than smoking (ie, hypertension, diabetes, dyslipidemia, hyperhomocysteinemia, and overweight) is significantly higher in patients with even mild renal failure than in those with normal renal function. Two circumstances may be responsible for this finding: CKD itself may in many cases lead to the development or to a worsening of traditional cardiovascular risk factors (in particular, the role of renal impairment must be considered in the development of secondary hypertension), and CKD may be a consequence of one or more underlying cardiovascular risk factors; regarding the latter point, it is worth noting the increasing importance of hypertension and diabetes mellitus as primary causes of ESRD worldwide. Besides traditional cardiovascular risk factors, CKD patients also are exposed to a number of conditions that are specific to CKD and that significantly contribute to the development of cardiovascular disease as well, also explaining why patients with CKD are exposed to a significantly higher annual mortality rate than patients with normal renal function, even after adjustment for blood pressure levels and other traditional cardiovascular risk factors. These CKD related cardiovascular risk factors include hemodynamic overload caused by plasma volume expansion and arterio venous fistula, anemia, disorders of calcium-phosphate metabolism, electrolyte imbalances, chronic inflammation, increased oxidant stress, hypercatabolism, and even uremia, which is characterized by the accumulation of potential cardio depressant toxins and an acceleration of both inflammatory and oxidant processes. Once patients start dialysis, their cardiovascular risk profile is increased by the exacerbation of pre-existing cardiovascular abnormalities owing to the decrease in the residual renal function. In addition, they are exposed to a number of additional risk factors related to the dialytic procedure itself, such as hemodynamic stresses caused by intra- and interdialytic changes in cardiac filling and fluctuations of blood pressure, rapid changes in serum electrolyte levels, bioincompatibility of membranes, and dialysate impurity. Considering the multiple cardiovascular risk factors operating in CKD patients, as well as the crucial role of their cardiovascular conditions on long-term outcome, it is mandatory that all available interventions aimed at the correction of all the modifiable risk factors potentially leading to the development of cardiovascular disease are performed as early as possible in the progression of the disease (P. Pozzoni et al. 20004).

2.6 Cardiovascular Disease in Chronic Kidney Disease: Risk Factors, Pathogenesis, and Prevention:

Chronic kidney disease (CKD) is one of the most common diseases worldwide. It is increasing in incidence and prevalence and affects at least 13% of the U.S. population. Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in CKD patients, occurring even at the earliest stages of CKD without manifest vascular disease. A graded increase in CVD risk occurs with worsening renal function. The cardiovascular (CV) mortality risk is substantially higher in dialysis patients than in an age-matched general population, CVD being the leading cause of death in individuals on dialysis. Updated guidelines have not only recognized CKD as an independent CV risk equivalent, but have also recommended that CKD be considered the highest risk group for subsequent development of CVD (4). The projected and actual burden of CKD has engendered controversy. According to the U.S. Renal Data System report published in 2013, 43% of patients with CKD and CVD had heart failure (HF), and 15% had a history of acute myocardial infarction (AMI); the equivalent proportions in non-CKD patients with CVD were 18.5% and 6.4% respectively. Among prevalent Medicare patients with CKD, 31% had HF, 11% had AMI, and 24% had atrial fibrillation. Cardiac death from arrhythmic mechanisms constituted the single largest cause of attributable mortality in both incident and prevalent patients with end-stage renal disease (ESRD). The pathogenesis of CVD in CKD patients is in some ways similar to that in patients without kidney disease. However, uremic toxins resulting from renal dysfunction play a significant role in the development CVD. Recognizing that factor is very important, because prevention of CV death is achieved not only by delaying the progression of CKD, but also by modifying CV risk factors early in the course of the disease (Ardhanari et al.2014).

2.7 Clinical Epidemiology of Cardiovascular Disease in Chronic Kidney Disease:

Cardiovascular disease (CVD) is the most common cause of death in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). The clinical epidemiology of CVD in CKD is challenging due to a prior lack of standardized definitions of CKD, inconsistent measures of renal function, and possible alternative effects of ‘traditional’ CVD risk factors in patients with CKD. These challenges add to the complexity of the role of renal impairment as the cause or the consequence of cardiovascular disease. The goal of this review is to summarize the current evidence on: (1) the incidence and prevalence of CVD in chronic renal insufficiency and in ESRD, (2) risk factors for CVD in CKD, (3) the outcomes of patients with renal failure with CVD, and (4) CKD as a risk factor for CVD. The epidemiological associations implicating the huge burden of CVD throughout all stages of CKD highlight the need to better understand and implement adequate screening, and diagnostic and treatment strategies. Reduced renal function has been estimated to affect almost 1 in 5 people in North America. Furthermore, renal impairment is associated with significant comorbidity that increases with progressive renal decline. Once an individual reaches end-stage renal disease (ESRD), cardiovascular disease (CVD) is responsible for approximately half of deaths. These individuals are 20 times more likely to have a cardiovascular-related death than for their kidneys to progressively fail to require dialysis or transplantation.

The clinical epidemiology of CVD in chronic kidney disease (CKD) is challenging due to a prior lack of standardized definitions of CKD and problems with the consistency of estimates of renal function. Another challenge has been 'reverse epidemiology' where the effects of 'traditional' CVD risk factors are different from those in the general population. In light of these challenges, the goal of this review is to summarize the current evidence on: (1) the incidence and prevalence of CVD in chronic renal insufficiency, (2) the incidence and prevalence of CVD in ESRD, (3) risk factors for CVD in CKD, (4) the outcomes of patients with renal failure with CVD, and (5) CKD as a risk factor for CVD. In this review, CKD is defined using NKF-DOQI guidelines and CVD encompasses coronary artery disease (CAD), cerebrovascular disease (CBVD), peripheral vascular disease (PVD), congestive heart failure (CHF), and left ventricular hypertrophy (LVH) (K. Kundhal C.E. Lok 2005).

2.8 Kidney Disease as a Risk Factor for Development of Cardiovascular Disease, A Statement From the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention:

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States, there is a rising incidence and prevalence of kidney failure, with poor outcomes and high cost. The number of individuals with kidney failure treated by dialysis and transplantation exceeded 320 000 in 1998 and is expected to surpass 650 000 by 2010. There is an even higher prevalence of earlier stages of CKD (Table 1). Kidney failure requiring treatment with dialysis or transplantation is the most visible outcome of CKD. However, cardiovascular disease (CVD) is also frequently associated with CKD, which is important because individuals with CKD are more likely to die of CVD than to develop kidney failure, CVD in CKD is treatable and potentially preventable, and CKD appears to be a risk factor for CVD. In 1998, the National Kidney Foundation (NKF) Task Force on Cardiovascular Disease in Chronic Renal Disease issued a report emphasizing the high risk of CVD in CKD. This 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. The task force recommended that patients with CKD be considered in the "highest risk group" for subsequent CVD events and that treatment recommendations based on CVD risk stratification should take into account the highest-risk status of patients with CKD. The major goal of this statement is to review CKD as a risk factor for development of CVD. As background, we shall also review the definition of CKD and classification of stages of severity of CKD, the spectrum of CVD in CKD and differences from the general population, and risk factors for CVD in CKD.

2.9 Novel markers of kidney function as predictors of end-stage kidney disease, cardiovascular disease and mortality in the general population:

Individuals with decreased kidney function are at substantially higher risk of mortality, cardiovascular disease and kidney failure than the general population. Cystatin C, a novel marker of kidney function, is more strongly associated with mortality and cardiovascular disease than is the traditionally-used serum creatinine. However, it is unknown if this is a specific property of cystatin C or whether strong associations with these adverse outcomes are shared by other novel kidney function markers, suggesting a greater potential for early detection and prevention.

It also is unclear whether the advantage of cystatin C, and potentially other novel markers, extends to prediction of kidney failure. Creatinine is a byproduct of muscle breakdown and, therefore, serum concentrations are affected by an individual's muscle mass. Equations accounting for age, race and sex improve the estimation of glomerular filtration rate (GFR) by accounting for average differences in muscle mass across these factors. Estimating equations, however, cannot account for individual differences in muscle mass for a given age, sex and race. Muscle wasting due to chronic illness is associated with lower creatinine generation, leading to a bias towards higher estimated GFR in such individuals. As these same individuals are at an elevated risk of mortality, this systematic bias results in an underestimate of the association between decreased GFR and mortality risk. In addition, renal tubular secretion of creatinine masks mildly decreased filtration, precluding early detection of disease. Cystatin C is less affected by muscle mass than serum creatinine, is not subject to tubular secretion, and is thought to be a better marker of early kidney dysfunction. Some reports, however, have shown that cystatin concentrations are affected by non-renal factors, including smoking, obesity and inflammation, which may be associated with increased risk themselves. Additional analytes, including the low molecular weight proteins β-trace protein (BTP) and β2 microglobulin (B2M), have recently been examined as alternative markers of kidney function. Several studies have reported correlations of BTP and B2M with directly measured GFR that are better or similar to those observed with creatinine. However, data on the putative associations between serum BTP or B2M concentrations with outcomes are limited. B2M, and to a lesser extent, BTP, share cystatin C′s advantage over eGFRcr in predicting outcomes, including kidney failure. These additional markers may be helpful in improving estimation of risk associated with reduced kidney function beyond current estimates based on eGFRcr (Brad C. Astor. 2012)

2.10 Outcome of Cardiovascular Disease In patients with Chronic Kidney Disease:

In 1997, the death rate from CVD (excluding CBVD) was approximately 22 times that from renal disease in the general population. A proportion of 40% of individuals with CKD will have a CVD-related death.

Mortality: Stages 1–4 The proportion of patients that will die due to cardiovascular disease is at least three times greater than that of patients who will die of renal disease. For example, in a randomized, multicenter prevention trial of 347,978 high-risk men with no CVD at baseline the crude rate of death from CAD was 23 times greater in blacks and 88 times greater in Caucasians than the death rate from renal disease. Individuals with established CVD have 3 times the CVD events and all-cause mortality compared with those without baseline CVD.

Mortality: Stage 5

The risk of cardiac events in patients who are dependent on dialysis or a kidney transplant is estimated to be between 3.5 and 50 times higher than in the general population. The annual mortality on dialysis is 20–23%, with cardiovascular causes accounting for 45% of these deaths. Furthermore, the prognosis after acute myocardial infarction is poor.

A recent, large population based study demonstrated 1- and 5 year mortality rates to be 59 and 90%, respectively that is 16–19 times higher compared with the general population. Likewise, transplant patients who develop de novo CAD or CHF have a 1.5–2.0 higher risk of death than nonrenal patients. Mortality after stroke is also increased. For patients who undergo cardiac revascularization, the in-hospital, 30-day and 1 year mortality was worse with greater degrees of renal impairment in a 26,500-patient cohort with a wide range of CKD.

2.11 Significance of the study

Cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD) is high, and the presence of CKD worsens outcomes of cardiovascular disease (CVD). CKD is associated with specific risk factors. Emerging evidence indicates that the pathology and manifestation of CVD differ in the presence of CKD. During a clinical update conference convened by the Kidney Disease: Improving Global Outcomes (KDIGO), an international group of experts defined the current state of knowledge and the implications for patient care in important topic areas, including coronary artery disease and myocardial infarction, congestive heart failure, cerebrovascular disease, atrial fibrillation, peripheral arterial disease, and sudden cardiac death. This survey was conducted to get actual picture of CVD in patients with CKD.

Chapter Three – Aim and Objectives

3. Aim and Objectives

The main objective of the present study was to investigate the "Prevalence of Cardiovascular Disease In patients with Chronic Kidney Disease in Some Hospitals of Dhaka".

The aims and objectives of the study were –

-To investigate prevalence of cardiovascular disease in chronic kidney disease patients
-To investigate how much CKD patients have cardiovascular disease or risk of cardiovascular disease.

Chapter Four – Materials and Methods

4.1 Type of study

The study was a survey based study.

4.2 Study area

We conducted our study in Kidney Foundation (Mirpur), National Kidney Institute (Mirpur Road), Ayesha Memorial Hospital (Mohakhali) & Department of Nephrology (BSMMU).

4.3 Inclusion Criteria

Here, male and female both patients were included. And only Indoor patients were included.

4.4 Exclusion Criteria

Outdoor patients were not included in this study.

4.5 Data collection paper

A data collection paper was made and compiled all the information and data of the patient in an organized manner.

4.6 Sample

A total of 172 CKD patient's data were collected from respective hospital & institute with their prio approval.

4.7 Statistical analysis

Data were organized, tabulated and aggregated using SPSS (Statistical Package for the Social Sciences). Distributive analysis of the health parameters was compared amongst the study population.

Chapter Five - Result

5.1. Demographic profile of participants:

5.1.1 Gender Distribution

Table: 5.1.1 – Gender Distribution

Sex	Number of Participants 172	
	Frequency	Percentage (%)
Male	107	61.05
Female	65	38.95

Number of Male participants was 107 and Female participants was 65.

5.1.2 Age Distribution

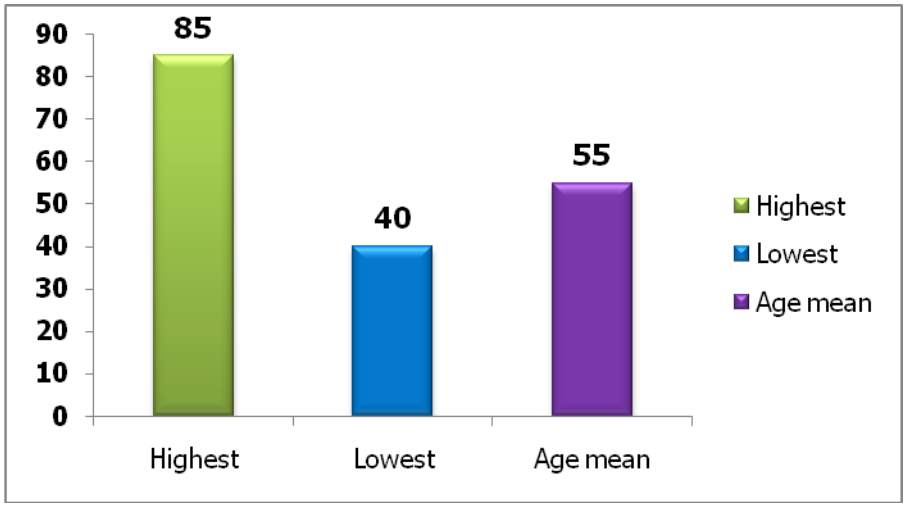

Figure:-1 Age Distribution of participants.

Highest age value was 85 and lowest age value was 40. Age mean was 55.

5.1.3 Occupational level of participants

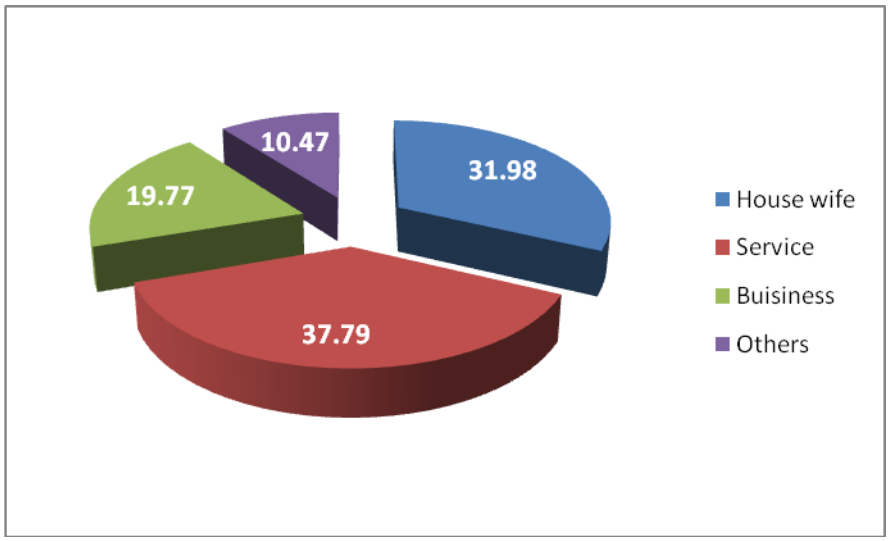

Figure:-2 Occupational level of participants.

Most of the patients were service holder (37.79%), house wife (31.98%) & business man (19.77%).

5.1.3 Marital status of participants

Table: 5.1.2 – Marital status of participants

Married	Widowed	Unmarried
86.05	12.21	1.74

Most of the patients were service holder (37.79%), house wife (31.98%) & business man (19.77%).

5.2. Behavioral data of participants:

5.2.1 Exercise habit of participants

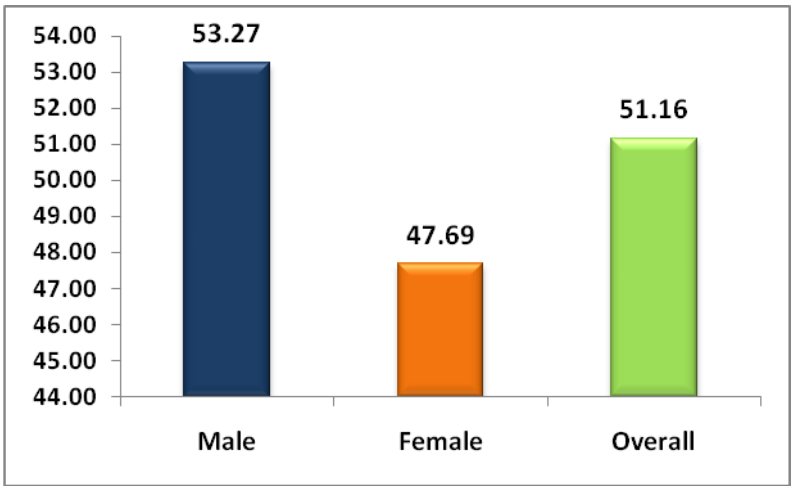

Figure:-3 Exercise habit of participants.

We found that No. of male & female patients doing physical exercise was 57 in 107 & 31out of 65.

5.2.2 Smoking habit of participants

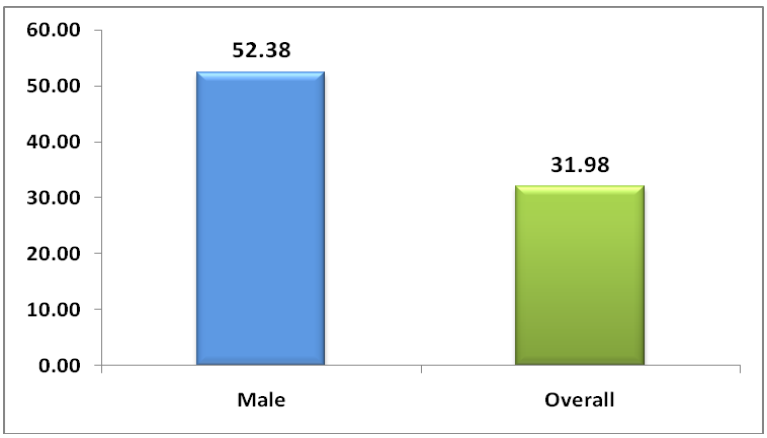

Figure:-4 Smoking habit of participants

We found that No. of male patients having smoking habit was 55 out of 107. None of the female patients were smoker.

5.2.3 Other habits of participants

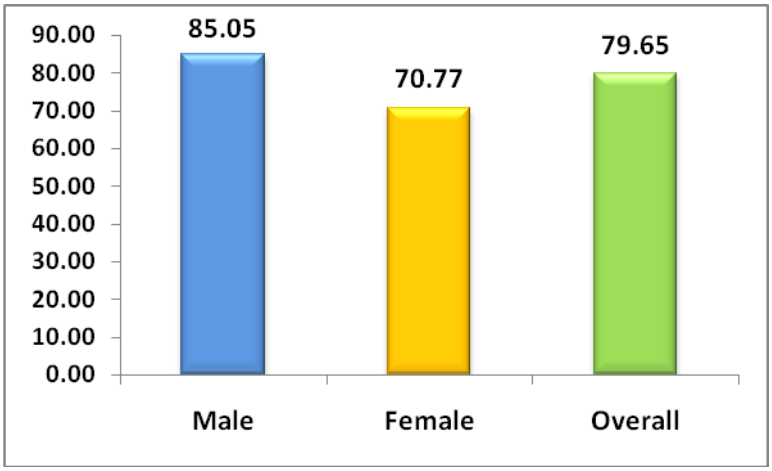

Figure:-5 Other habits of participants

We found that No. of male & female patients having other habits (Coffee/Tea/Soda) was 91 in 107 & 46 out of 65.

5.3. History of other diseases:

5.3.1 Patients having Hypertension

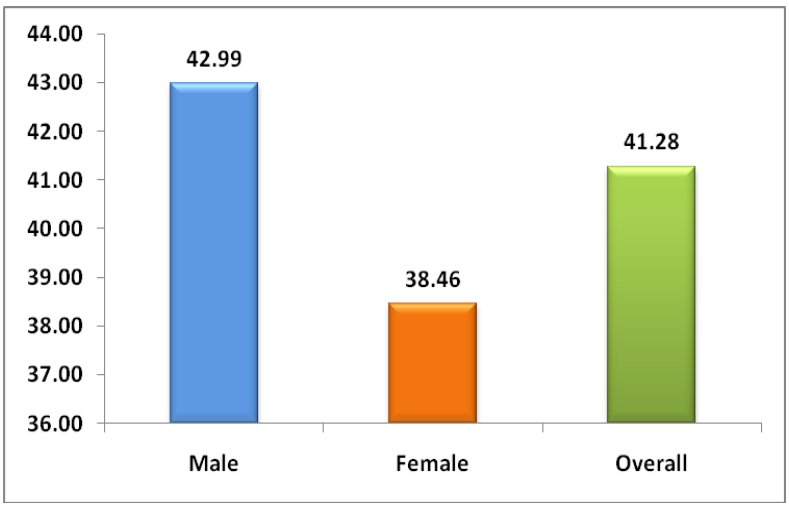

Figure:-6 Patients having Hypertension

We found that No. of male & female patients having **Hypertension** was 46 in 107 & 25 out of 65.

5.3.2 Patients having Asthma/COPD

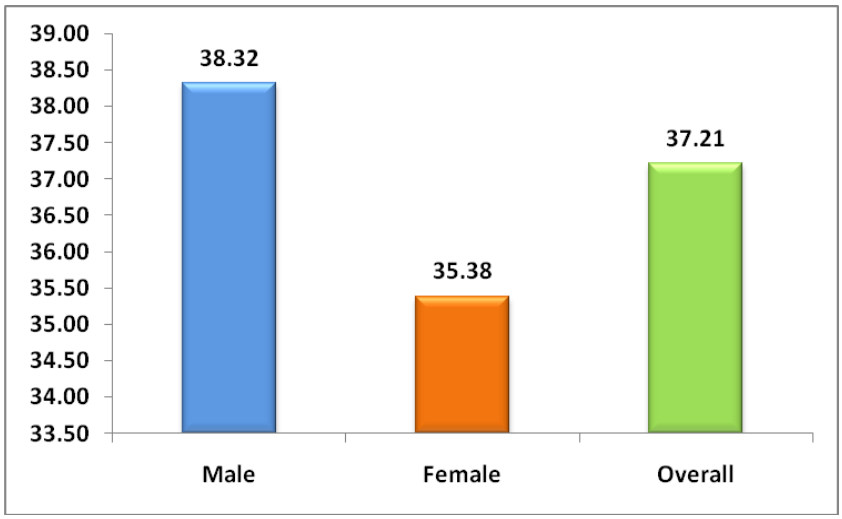

Figure:-7 Patients having Asthma/COPD

We found that No. of male & female patients having Asthma/COPD was 41 in 107 & 23 out of 65.

5.3.3 Patients having Diabetes

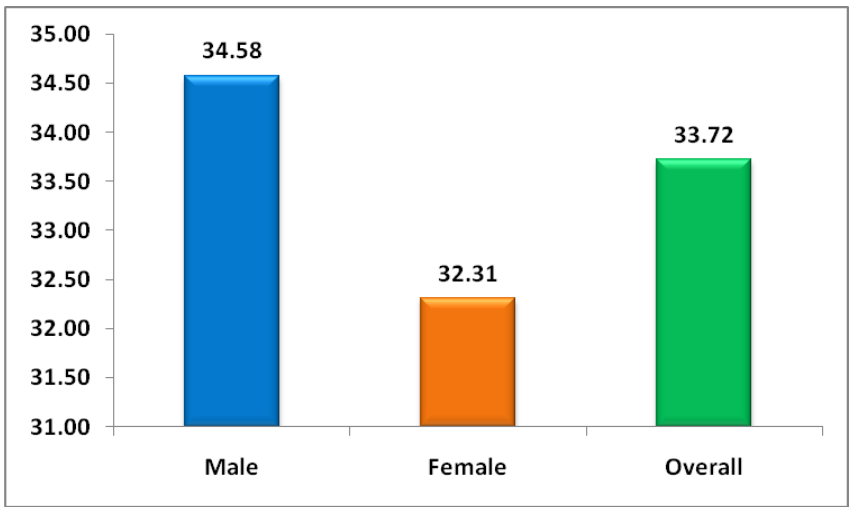

Figure:-8 Patients having Diabetes

We found that No. of male & female patients having Diabetes was 37 in 107 & 21 out of 65.

5.3.4 Stage wise CKD Patient Distribution

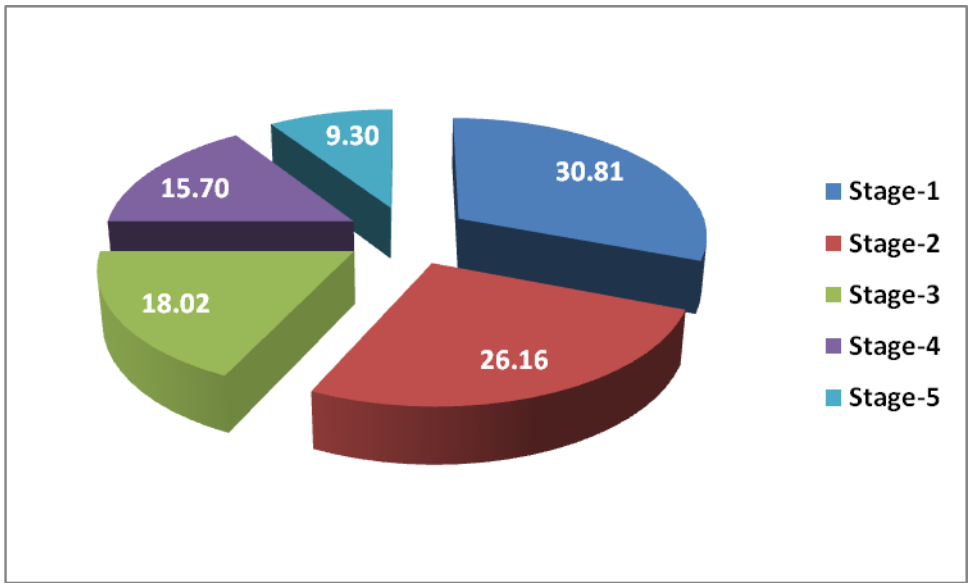

Figure:-9 Stage wise CKD Patient Distribution

We found that patients having CKD stage 4 & 5 and requiring dialysis about 21.51%.

5.4 Prevalence of CVD in CKD patients

5.4.1 Prevalence of Atherosclerotic heart disease (ASHD) in CKD patients:

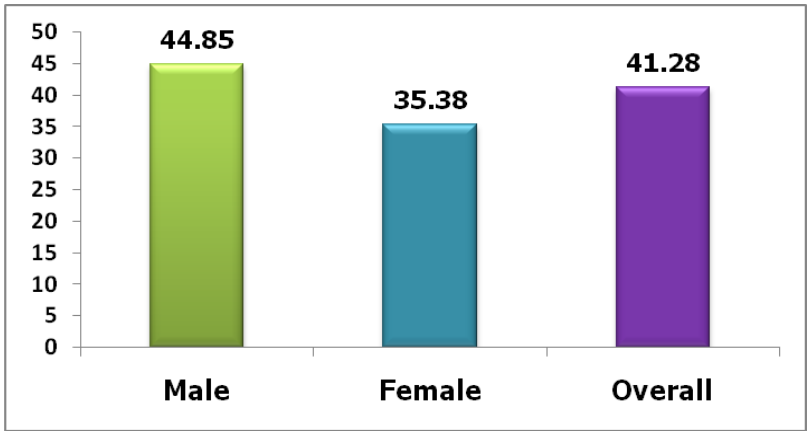

Figure:-10 Prevalence of ASHD in CKD patients

We found that No. of male & female patients having ASHD was 48 in 107 & 23 out of 65.

5.4.2 Prevalence of Acute myocardial infarction (AMI) in CKD patients:

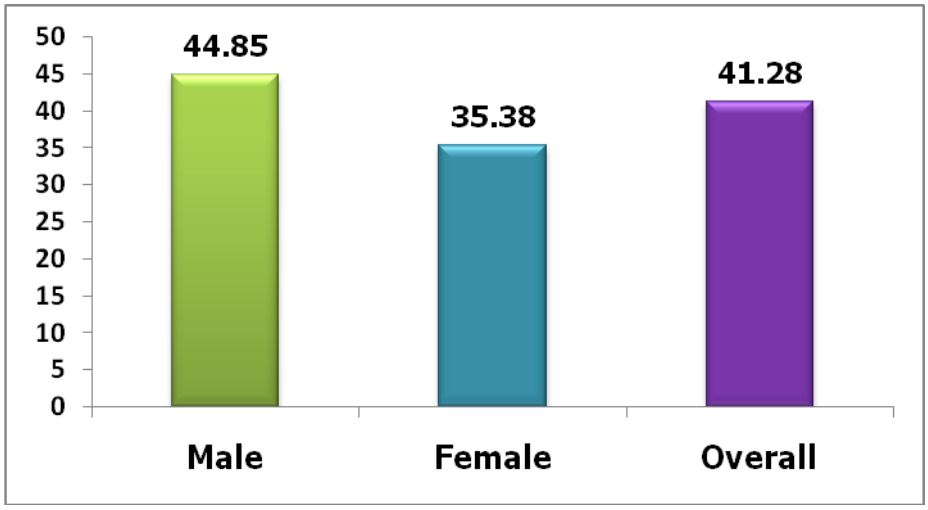

Figure:-11 Prevalence of AMI in CKD patients

We found that No. of male & female patients having AMI was 13 in 107 & 6 out of 65.

5.4.3 Prevalence of Congestive heart failure (CHF) in CKD patients:

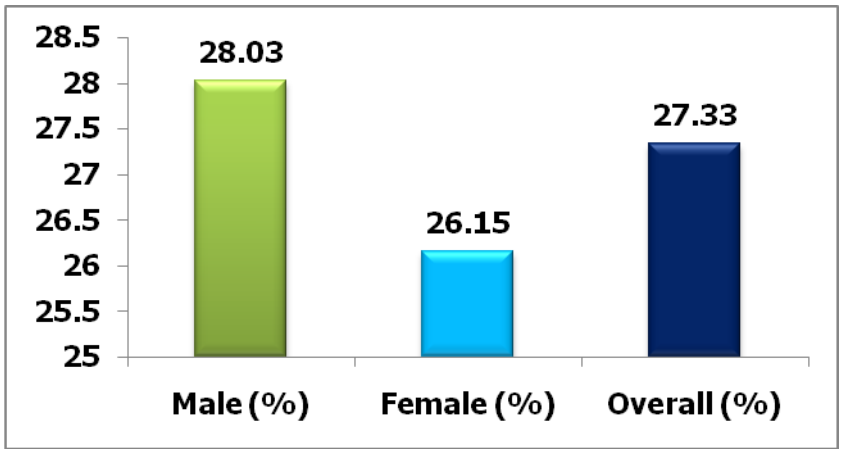

Figure:-12 Prevalence of CHF in CKD patients

We found that No. of male & female patients having CHF was 30 in 107 & 17 out of 65.

5.4.4 Prevalence of Peripheral artery disease (PAD) in CKD patients:

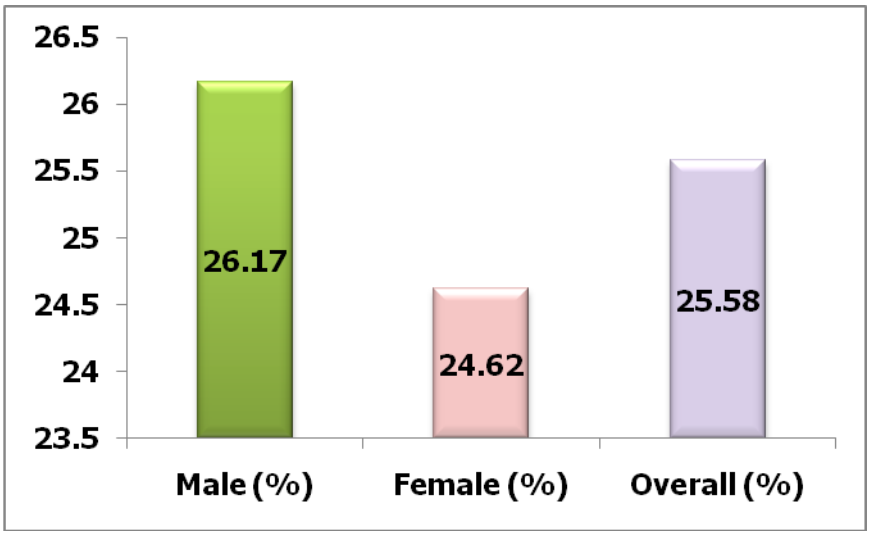

Figure:-13 Prevalence of PAD in CKD patients

We found that No. of male & female patients having CHF was 28 in 107 & 16 out of 65.

Chapter Six - Conclusion

CKD is a major health burden; the presence of CKD appears to be an independent risk factor for CVD outcomes, particularly in higher-risk populations. Beside those patients with CKD should be considered in the highest-risk group for CVD events. Prevalence of CVD in patients with CKD in Bangladesh is very high. Being an underdeveloped country Bangladeshis are at high risk of CVD with CKD because of their lack of knowledge. Beside those, our healthcare facilities are not also available to the poorer patients. So, most of the time CVD with CKD remains undiagnosed or diagnosed at the 11^{th} hour. More study requires to measure overall nationwide picture.

Chapter Seven – Discussion

The main objective of the present study was to investigate prevalence of cardiovascular disease in patients with chronic kidney disease in some hospitals of Dhaka.

. To measure prevalence a data collection paper was made and compiled all the information & the data of the patient in an organized manner.

Two aims and objective were formulated to test in this study. First posits to investigate prevalence of cardiovascular disease in chronic kidney disease patients & how much CKD patients have cardiovascular disease or risk of cardiovascular disease. A total of 172 CKD patient's data were collected from reputed hospitals.

In the study we found that prevalence of CVD in patients with CKD is very high in Bangladesh. Prevalence of Atherosclerotic heart disease (ASHD) in CKD patients was 41.28%. Male patients having ASHD was 44.85% (48 persons out of 107). Female most patients having ASHD was 38.38% (23 persons out of 65). Which was comparable with a report on US people prevalence of ASHD in patients without CKD were 16.5 which have been increased to 41.5% in patients with CKD.

Prevalence of Acute myocardial infarction (AMI) in CKD patients was 11.05%. Male patients having AMI was 12.15% (13 persons out of 107). Female most patients having AMI was 9.23% (6 persons out of 65). Which was comparable with US people, in that case prevalence of AMI in patients without CKD was only 2.3% which has been increased to 15.1% in patients with CKD.

Prevalence of Congestive heart failure (CHF) in CKD patients was 27.33%. Male patients having CHF was 28.03% (30 persons out of 107). Female most patients having CHF was 26.15% (17 persons out of 65).

Which was comparable with a report on US people, in that case prevalence of CHF in patients without CKD was only 6.4% which have been increased to 38.8% in patients with CKD.

Prevalence of Peripheral artery disease (PAD) in CKD patients was 25.58%. Male patients having PAD was 26.16% (28 persons out of 107). Female most patients having PAD was 24.62% (16 persons out of 65). As per a report on US people prevalence of PAD in patients without CKD was only 8.9% which has been increased to 25.8% in patients with CKD.

Beside those we have measured the presence of hypertension & diabetes in CKD patients and result was 41.28 (hypertension) & 33.72 in case of (diabetes).

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