ASSOCIATION OF CHRONIC KIDNEY DISEASE WITH DIABETES MELLITUS: A SURVEY ON ITS PREVALENCE, TREATMENT PATTERN, AND RISK FACTORS IN CONTEX OF BANGLADESH.



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This Thesis Paper is dedicated to MY FAMILY

Declaration by the Research Candidate

I, Istiak Jahan hereby declare that the dissertation entitled "Association of Chronic kidney disease with Diabetes mellitus: A survey on its prevalence, treatment pattern, and risk factors in context of Bangladesh" submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, under the supervision and guidance of Marjana Khalil, Lecturer, Department of Pharmacy, East West University. The thesis paper has not formed the basis for the award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

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This is to certify that the dissertation entitled "Association of Chronic kidney disease with Diabetes mellitus: A survey on its prevalence, treatment pattern, and risk factors in context of Bangladesh" submitted to the department of pharmacy, East West University, Dhaka, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy, was carried out by Istiak Jahan (ID: 2013-1-70-055) under my supervision and no part of the research has been submitted for any other degree. The thesis has not dissertion has been or is being submitted elsewhere for award of any other degree/diploma/fellowship.

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This is to certify that the thesis entitled "Association of Chronic kidney disease with Diabetes mellitus: A survey on its prevalence, treatment pattern, and risk factors in context of Bangladesh" is a record of original and genuine research work carried out by Istiak Jahan, under my supervision of Marjana Khalil (Lecturer, Department of Pharmacy, East West University). I further certify that no part of this thesis has been submitted for any other degree and all the resources of the information in this connection are duly acknowledged.

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Abstract

Diabetes mellitus is a growing epidemic and is one of the most common causes of chronic kidney disease (CKD) and kidney failure. Large epidemiological studies have shown that one third of the patients on hemodialysis or renal transplant recipients are diabetics, predominantly with type 2 diabetes. Based on this evidence the aim of this survey work was to determine the association of chronic kidney disease with diabetes mellitus in the context of Bangladesh. About 144 patients were interviewed on the predetermined questionnaire set on the objectives of this survey work. The survey was conducted at two branches of BIRDEM hospital in Dhaka city city: Rampura centre and Jurain centre. The majority of the survey population was female which contributes around 60% of the population and 40% was male. Patients aged from 45 to 64, highly suffers from diabetes mellitus and the prevalence is around 57%. The second highest group of patients was aged above 54, where the prevalence is around 23% and 29% patient group came from the age above 65. The socio-economic condition of the patients was mostly average: 58% patients were from middle class, 29% people were from upper-middle class, and 13% were from poor economical status out of 144 samples. According to this survey study people who are suffering from diabetic mellitus for 5 or more years have the highest chance of developing chronic kidney disease. These finding gave the indication that chronic kidney disease is associated with long term diabetes mellitus. This research also evaluated the treatment pattern of both diseases. Patients with diabetes mellitus mostly treated with oral anti-diabetic agent besides insulin. Also this study result proves diabetes as the leading risk factors for chronic kidney diseases which accounts for 48%. it is seen that majority of the patient (48%) had the HbA1C level in between 7% to 9%. Secondly, 42% patient had their HbA1C level in below 7%. And 5% patient had the HbA1C level in between 10% to 14% and the remaining 5% had above 14%. Creatinine level of the chronic kidney disease patients were about (1.6-2.5) ml\dl in the majority patients (32.6%), 1-1.5 ml/dl in the 29% patients & 0.5-0.9 ml/dl in the 28.5% patients. In summary, this survey work gave us an updated review on the growing public health burden of chronic kidney disease associated with diabetes mellitus in the Dhaka city.

Key Words: Diabetes mellitus, Chronic kidney disease, HbA1C, Creatinine, Prevalence

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Abbreviation

CKD: Chronic kidney disease DM: Diabetes mellitus GFR: Glomerular filtration rate GDM: Gestational diabetes mellitus IDDM: Insulin-dependent diabetes mellitus IGT: Impaired glucose tolerance IFG: Impaired fasting glucose BUN: Blood urea nitrogen DPP-4: Dipeptidyl peptidase-4 inhibitor GLP-1: Glucagon-like peptide-1

SGLT2 inhibitors: Sodium-glucose co-transporter 2 inhibitors

In 2012 around 56 million people died throughout the world. Among of them 120,000 people were war killed and another 500,000 were crime killed (UNDOC, 2013). In contrast 1.5 million people died on diabetes (WHO, 2013). So, diabetes is now more dangerous than war.

Diabetic is becoming the leading cause of chronic kidney disease (CKD) and kidney failure in Bangladesh. Chronic kidney disease is the decreased glomerular filtration rate (GFR) or albuminuria, or both which can lead to devastating complication. A variety of forms of kidney disease can be seen in people with diabetes, including diabetic nephropathy, ischemic damage related to vascular disease and hypertension, as well as other renal diseases.

1.1 Diabetes mellitus

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic diseases characterized by hyperglycemic condition due inability of pancreas to yield sufficient insulin or the decreased ability of body to effectively use insulin it produces.

The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Several pathogenic processes are involved in the development of diabetes such as autoimmune destruction of the β -cells of the pancreas which result in insulin deficiency, abnormalities with consequent resistance to insulin action etc. Deficient insulin action can be due to either inadequate insulin secretion or cells of the body do not response properly to insulin. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality is the primary cause of the hyperglycemia (American Diabetes Association, 2004)

1.2 Description of Diabetes Mellitus (DM)

There are three main types of diabetes mellitus: Type 1 DM, Type 2 DM and Gestational diabetes.

> Type 1 DM:

It results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". IT is called juvenile diabetes because this form develops most frequently in children and adolescents and the cause is unknown. Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas. This type can be further classified as immune-mediated or idiopathic. (WHO, 2010)

According to American Diabetes Association (2004) immune-mediated diabetes account for (5-10)% type 1 diabetes mellitus cases. It results from a cellular-mediated autoimmune destruction of the β -cells of the pancreas. Markers of the immune destruction of the β -cell include islet cell autoantibodies, autoantibodies to insulin, autoantibodies to glutamic acid decarboxylase (GAD65), and autoantibodies to the tyrosine phosphatases IA-2 and IA-2 β .

In this form of diabetes, the rate of β -cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults). Some patients, particularly children and adolescents, may present with ketoacidosis as the first manifestation of the disease. Autoimmune destruction of β -cells has multiple genetic predispositions and is also related to environmental factors that are still poorly defined. Although patients are rarely obese when they present with this type of diabetes, the presence of obesity is not incompatible with the diagnosis. These patients are also prone to other autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis, Addison's disease, vitiligo, celiac sprue, autoimmune hepatitis, myasthenia gravis, and pernicious anemia.

Idiopathic diabetes has no known etiologies. Some of these patients have permanent insulinopenia and are prone to ketoacidosis, but have no evidence of autoimmunity. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for β -cell autoimmunity.

> Type 2 DM:

Type 2 diabetes (non-insulin-dependent diabetes) which results from the body's inability to respond properly to the action of insulin produced by the pancreas. Type 2 diabetes is much

more common and accounts for around 90% of all diabetes cases worldwide. It occurs most frequently in adults, but is being noted increasingly in adolescents as well (WHO, 2010).

In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, high blood sugar can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce the liver's glucose production.

Type 2 DM is due to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 DM, including obesity, lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Even those who are not obese often have a high waist–hip ratio (Elsevier, 2016).

| Features | Type 1 diabetes | Type 2 diabetes |
|-----------------------------------|--------------------|-----------------------------------|
| Onset | Sudden | Gradual |
| Age at onset | Mostly in children | Mostly in adults |
| Body size | Thin or normal | Often obese |
| Ketoacidosis | Common | Rare |
| Autoantibodies | Usually present | Absent |
| Endogenous insulin | Low or absent | Normal, decreased or increased |
| Concordance in identical twins | 50% | 90% |
| Prevalence | ~10% | ~90% |

(Melmed et al., 2011)

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Gestational diabetes:

GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy. Deterioration of glucose tolerance occurs normally during pregnancy, particularly in the 3rd trimester(American Diabetes Association, 2004)

Pregnant women who have an increased risk of developing gestational diabetes include those who:

- Are over 25 years old
- Are above their desired body weight
- Have a family history of diabetes

Usually, blood glucose levels return to normal after childbirth. However, women who have had gestational diabetes have an increased risk of developing type 2 diabetes later in life (Cleveland Clinic, 1995).

1.3 Impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) refer to levels of blood glucose concentration above the normal range, but below those which are diagnostic for diabetes. Subjects with IGT and/or IFG are at substantially higher risk of developing diabetes and cardiovascular disease than those with normal glucose tolerance (WHO, 2004)

The Expert Committee recognized an intermediate group of subjects whose glucose levels, although not meeting criteria for diabetes, are nevertheless too high to be considered normal. This group is defined as having fasting plasma glucose (FPG) levels $\geq 100 \text{ mg/dl}$ (5.6 mmol/l) but <126 mg/dl (7.0 mmol/l) or 2-h values in the oral glucose tolerance test (OGTT) of $\geq 140 \text{ mg/dl}$ (7.8 mmol/l) but <200 mg/dl (11.1 mmol/l). Thus, the categories of FPG values are as follows:

- FPG <100 mg/dl (5.6 mmol/l) = normal fasting glucose;
- FPG 100–125 mg/dl (5.6–6.9 mmol/l) = IFG (impaired fasting glucose);

• FPG \geq 126 mg/dl (7.0 mmol/l) = provisional diagnosis of diabetes.

The corresponding categories when the OGTT is used are the following:

- 2-h postload glucose <140 mg/dl (7.8 mmol/l) = normal glucose tolerance;
- 2-h postload glucose 140–199 mg/dl (7.8–11.1 mmol/l) = IGT (impaired glucose tolerance);
- 2-h postload glucose $\geq 200 \text{ mg/dl} (11.1 \text{ mmol/l}) = \text{provisional diagnosis of diabetes.}$

Patients with IFG and/or IGT are now referred to as having "pre-diabetes" indicating the relatively high risk for development of diabetes in these patients. In the absence of pregnancy, IFG and IGT are not clinical entities in their own right but rather risk factors for future diabetes as well as cardiovascular disease. IFG and IGT are associated with the metabolic syndrome, which includes obesity (especially abdominal or visceral obesity), dyslipidemia of the high-triglyceride and/or low-HDL type, and hypertension. It is worth mentioning that medical nutrition therapy aimed at producing 5–10% loss of body weight, exercise, and certain pharmacological agents have been variably demonstrated to prevent or delay the development of diabetes in people with IGT; the potential impact of such interventions to reduce cardiovascular risk has not been examined to date.

Note that many individuals with IGT are euglycemic in their daily lives. Individuals with IFG or IGT may have normal or near normal glycated hemoglobin levels. Individuals with IGT often manifest hyperglycemia only when challenged with the oral glucose load used in the standardized OGTT (American Diabetes Association, 2004).

1.4 Cause of Diabetes Mellitus

Some cases of diabetes are caused by the body's tissue receptors not responding to insulin (evenwhen insulin levels are normal, which is what separates it from type 2 diabetes); this form is

very uncommon. Genetic mutations (autosomal or mitochondrial) can lead to defects in beta cell function. Abnormal insulin action may also have been genetically determined in some cases. Any disease that causes extensive damage to the pancreas may lead to diabetes (for example, chronic pancreatitis and cystic fibrosis).Diseases associated with excessive secretion of insulin-antagonistic hormones can cause diabetes(which is typically resolved once the hormone excess is removed). Many drugs impair insulin secretion and some toxins damage pancreatic beta cells(National institute of diabetes and digestive and kidney diseases, 2014).

Drugs that cause of Diabetes Mellitus

- Glucocorticoids
- Thyroid hormone
- β-adrenergic agonists
- Statin (Sattar et al., 2010)

1.5 Risk Factors for Type 2 Diabetes

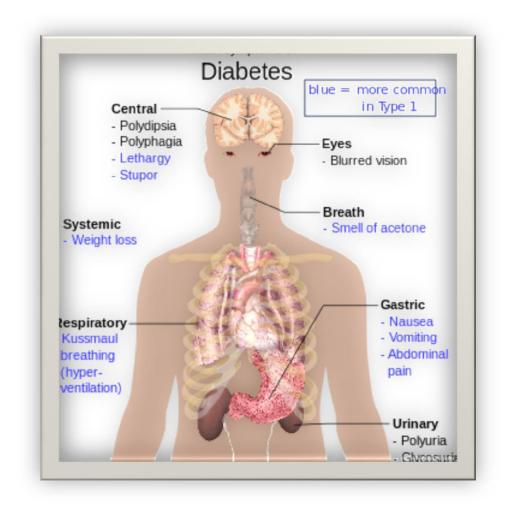
People who develop type 2 diabetes are more likely to have the following characteristics:

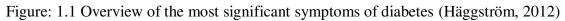
- Age 45 or older
- Overweight or obese
- Physically inactive
- Parent or sibling with diabetes
- Family history
- History of giving birth to a baby weighing more than 9 pounds
- History of gestational diabetes
- High blood pressure—140/90 or above—or being treated for high blood pressure
- High-density lipoprotein (HDL), or good, cholesterol below 35 milligrams per deciliter(mg/dL), or a triglyceride level above 250 mg/dL
- Polycystic ovary syndrome, also called PCOS
- Insulin resistance
- Impaired glucose tolerance.

(American Diabetes Association, 2013)

1.6 Signs and symptoms

The classic symptoms of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 DM, while they usually develop much more slowly and may be subtle or absent in type 2 DM.





Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurry vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number

of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes (WHO, 2014).

1.7 Treatment of Diabetes mellitus

Treatment of type 1 Diabetes mellitus

Type 1 diabetes can only be treated with insulin, typically with a combination of regular and NPH insulin, or synthetic insulin analogs.

Treatment of type 2 Diabetes mellitus

Some people who have type 2 diabetes can achieve their target blood sugar levels with diet and exercise alone, but many also need diabetes medications or insulin therapy.

Examples of possible treatments for type 2 diabetes include:

Metformin: Generally, metformin is the first medication prescribed for type 2 diabetes. It works by improving the sensitivity of body tissues to insulin so that body uses insulin more effectively.

Metformin also lowers glucose production in the liver. Metformin usually won't lower blood sugar enough on its own. Doctor will also recommend lifestyle changes, such as losing weight and becoming more active.

Nausea and diarrhea are possible side effects of metformin. These side effects usually go away as body gets used to the medicine. If metformin and lifestyles changes aren't enough to control blood sugar level, other oral or injected medications can be added.

Sulfonylureas: These medications help body secrete more insulin. Examples of medications in this class include glyburide, glipizide and glimepiride (Amaryl). Possible side effects include low blood sugar and weight gain.

Meglitinides: These medications work like sulfonylureas by encouraging the body to secretemore insulin, but they're faster acting, and they don't stay active in the body for as long.

They also have a risk of causing low blood sugar, but not as much risk as sulfonylureas do. Weight gain is a possibility with this class of medications as well. Examples include repaglinideand nateglinide.

Thiazolidinediones: Like metformin, these medications make the body's tissues more sensitive to insulin. This class of medications has been linked to weight gain and other more serious side effects, such as an increased risk of heart failure and fractures. Because of the risks, these medications generally aren't a first-choice treatment. Rosiglitazone and pioglitazone are examples of thiazolidinediones.

DPP-4 inhibitors: These medications help reduce blood sugar levels, but tend to have a modest effect. They don't seem to cause weight gain.

Examples of these medications are sitagliptin, saxagliptin and linagliptin

GLP-1 receptor agonists: These medications slow digestion and help lower blood sugar levels, though not as much as sulfonylureas. This class of medications isn't recommended for use alone.

Exenatide and liraglutide are examples of GLP-1 receptor agonists.

Possible side effects include nausea and an increased risk of pancreatitis.

SGLT2 inhibitors: These are the newest diabetes drugs on the market. They work by preventing the kidneys from reabsorbing sugar in the blood. Instead, the sugar is excreted in the urine.

Examples include canagliflozin and dapagliflozin.

Side effects may include yeast infections and urinary tract infections.

(Drugs.com, 2000)

Insulin therapy: Some people who have type 2 diabetes need insulin therapy as well. In the past, insulin therapy was used as last resort, but today it's often prescribed sooner because of its benefits.

Because normal digestion interferes with insulin taken by mouth, insulin must be injected. Depending on needs, doctor may prescribe a mixture of insulin types to use throughout the day and night. Often, people with type 2 diabetes start insulin use with one long-acting shot at night. Insulin injections involve using a fine needle and syringe or an insulin pen injector — a device that looks similar to an ink pen, except the cartridge is filled with insulin.

There are many types of insulin, and they each work in a different way. Options include:

- Insulin glulisine
- Insulin lispro
- Insulin aspart
- Insulin glargine (Lantus)
- Insulin isophane

(Cleveland Clinic, 2000)

1.8 Chronic kidney disease

Chronic kidney disease (CKD), also known as chronic renal disease, is a progressive loss in renal function over a period of months or years. The symptoms of worsening kidney function are not specific, and might include feeling generally unwell and experiencing a reduced appetite. Often, chronic kidney disease is diagnosed as a result of screening of people known to be at risk of kidney problems, such as those with high blood pressure or diabetes and those with a blood relative with CKD (Uhlig et al., 2010).

Chronic renal failure (CRF) is a progressive disease characterized by an increasing inability of the kidney to maintain normal low levels of the products of

- Protein metabolism (such as urea)
- Normal blood pressure
- Hematocrit
- Sodium
- Water
- Potassium
- Acid-base balance.

This disease may also be identified when it leads to one of its recognized complications, such as cardiovascular disease, anemia. It is differentiated from acute kidney disease in that the reduction in kidney function must be present for over 3 months. Chronic kidney disease is identified by a blood test for creatinine, which is a breakdown product of muscle metabolism. Higher levels of creatinine indicate a lower glomerular filtration rate and as a result a decreased capability of the kidneys to excrete waste products. Creatinine levels maybe normal in the early stages of CKD, and the condition is discovered if urinalysis (testing of a urine sample) shows the kidney is allowing the loss of protein or red blood cells into the urine. To fully investigate the underlying cause of kidney damage, various forms of medical imaging, blood tests, and sometimes a renal biopsy (removing a small sample of kidney tissue) are employed to find out if a reversible cause for the kidney malfunction is present.

Renal function is clinically monitored by measurement of

- Serum creatinine
- Blood urea nitrogen (BUN)
- Urinalysis.

Once serum creatinine in an adult reaches about 3 mg/dLRenal disease are irreversible and progress to end-stage renal disease (ESRD).

In patients with an elevated serum creatinine level (1.5 to 3.0 mg/dL), the term chronic renal insufficiency is useful and implies that progression to CRF and ESRD is not inevitable (Andrassy, 2013).

1.9 Causes of CKD:

The two main causes of chronic kidney disease are diabetes and high blood pressure, which are responsible for up to two-thirds of the cases. Diabetes happens when blood sugar is too high, causing damage to many organs in body, including the kidneys and heart, as well as blood vessels, nerves and eyes. High blood pressure, or hypertension, occurs when the pressure of blood against the walls of blood vessels increases. If uncontrolled, or poorly controlled, high blood pressure can be a leading cause of heart attacks, strokes and chronic kidney disease. Also, chronic kidney disease can cause high blood pressure. Other conditions that affect the kidneys are:

- Glomerulonephritis, a group of diseases that cause inflammation and damage to the kidney's filtering units. These disorders are the third most common type of kidney disease.
- Inherited diseases, such as polycystic kidney disease, which causes large cysts to form in the kidneys and damage the surrounding tissue.
- Malformations that occur as a baby develops in its mother's womb. For example, anarrowing may occur that prevents normal outflow of urine and causes urine to flow backup to the kidney. This causes infections and may damage the kidneys.
- Lupus and other diseases that affect the body's immune system.
- Obstructions caused by problems like kidney stones, tumors or an enlarged prostate gland in men.
- Repeated urinary infections.

(National Kidney Foundation, 2016)

1.10 Symptoms of CKD:

Most people may not have any severe symptoms until their kidney disease is advanced. However, you may notice that you:

- feel more tired and have less energy
- have trouble concentrating
- have a poor appetite
- have trouble sleeping
- have muscle cramping at night

- have swollen feet and ankles
- have puffiness around your eyes, especially in the morning
- have dry, itchy skin
- need to urinate more often, especially at night.

Anyone can get chronic kidney disease at any age. However, some people are more likely than others to develop kidney disease. You may have an increased risk for kidney disease if you:

- have diabetes
- have high blood pressure
- have a family history of kidney failureare older

(National Kidney Foundation, 2016)

1.11 Stages:

All individuals with a glomerular filtration rate (GFR) <60 ml/min/1.73 m2 for 3 months are classified as having chronic kidney disease, irrespective of the presence or absence of kidney damage. The rationale for including these individuals is that reduction in kidney function to this level or lower represents loss of half or more of the adult level of normal kidney function, which may be associated with a number of complications such as the development of cardiovascular disease

| CKD Stage | GFR level (mL/min/1.73 m^2) |
|-----------|--------------------------------|
| Stage 1 | \geq 90 |
| Stage 2 | 60 - 89 |
| Stage 3 | 30 - 59 |
| Stage 4 | 15 - 29 |
| Stage 5 | < 15 |

(Healthwise, 1995)

• Description of stages are-

➢ Stage 1-

Slightly diminished function; kidney damage with normal or relatively high GFR (≥90 ml/min/1.73 m²). Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

➢ Stage 2-

• Mild reduction in GFR (60–89 ml/min/1.73 m²) with kidney damage. Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Stage 3-

• Moderate reduction in GFR (30–59 ml/min/1.73 m²).

Stage 4-

• Severe reduction in GFR (15–29 ml/min/1.73 m²) Preparation for renal replacement therapy.

➢ Stage 5-

• Established kidney failure (GFR <15 ml/min/1.73 m²), permanent renal replacement therapy, or end-stage kidney disease.

(Healthwise, 1995)

GFR- GFR is a measurement of how many millimeters (ml) of waste fluid kidneys can filter from the blood in a minute (measured in ml/min) (National Kidney Foundation, 2016).

1.12 Pathophysiology of CKD:

Patients are often not seen until late in the course of the disease, when much of their kidney function has already been lost Kidney adapts so well to progressive loss of nephrons and can maintain constancy of the internal environment until about 75% of renal function has been lost. Patients with uremic manifestations can have a myriad of different complaints referable to almost any organ system.

There are many diseases that cause chronic renal disease; each has its own pathophysiology. However, there are common mechanisms for disease progression.

- Pathologic features include fibrosis, loss of renal cells, and infiltration of renal tissue by monocytes and macrophages.
- Proteinuria, hypoxia, and extensive angiotensin II production all contribute to the pathophysiology. In an attempt to maintain GFR, the glomerular hyperfiltration; this results in endothelial injury.
- Proteinuria results from increased glomerular permeability and increased capillary pressure.

Hypoxia also contributes to disease progression. Angiotensin II increases glomerular hypertension, which further damages the kidney.

- The major cause of the failure to excrete enough acid is diminished renal ammonia production and excretion.
- In the gastrointestinal tract, anorexia and morning vomiting are common.
 - ✓ In severe uremia, gastrointestinal bleeding may occur secondary to platelet dysfunction and diffuse mucosal erosions throughout the gut.
 - \checkmark Bloody diarrhea can occur secondary to uremic colitis.
- Heart failure is common and is due to sodium and water retention, acid-base changes, hypocalcemia and hyperparathyroidism, hypertension, anemia, coronary artery disease, and diastolic dysfunction secondary to increased myocardial fibrosis with oxalate and urate deposition and myocardial calcification. Uremia itself may also impair myocyte function.

- Neuromuscular abnormalities with asterixis and muscle twitching are common, as are muscle cramps.
- Progressively more severe normochromic, normocytic anemia develops as the GFR and renal erythropoietin secretion decrease.
 - ✓ In most patients, the hematocrit reaches about 20 to 25% by the time that ESRD develops.
- Hypertension
 - ✓ Hypertension develops in 95% of patients with CRF before ESRD does.
 - ✓ If untreated, this type of hypertension is much more likely to enter the malignant phase than is essential hypertension.
- It is characterized by a prolonged bleeding time but usually normal prothrombin and partial thromboplastin times, platelet count, and clotting time.
- As uremia progresses, subtle mental and cognitive dysfunction develops and, if untreated, progresses to coma.
- Pruritus is a common and troublesome complication of uremia that is only partially explained by hyperparathyroidism.

(Belleza, 2016)

1.13 Treatment of CKD:

1.13.1 Angiotensin-converting enzyme inhibitor:

There are several types and brands of this type of medication. Angiotensin-converting enzyme(ACE) inhibitors work by reducing the amount of a chemical called angiotensin II that you make in your bloodstream. This chemical tends to narrow (constrict) blood vessels. Therefore, less of this chemical causes the blood vessels to relax and widen, and so the pressure of blood within the blood vessels is reduced.

ACE inhibitors are drugs that are often used to treat high blood pressure. However, the way theywork also seems to have a protective effect on the kidneys and heart. This means that they help to prevent or delay the progression of the kidney disease (Healthwise, 2016).

1.13.2 Angiotensin-II receptor antagonist:

There are several types and brands of this type of medication. Angiotensin-II receptor antagonists (AIIRAs) work in a similar way to ACE inhibitors. One may be used instead of anACE inhibitor if have problems or side-effects with taking an ACE inhibitor. For example, some people taking an ACE inhibitor develop a persistent cough (Healthwise ,2016).

1.13.3 Diuretic:

According to Drugs.com (2000), a diuretic is any substance that promotes the production of urine. This includes forced diuresis. There are several categories of diuretics. All diuretics increase the excretion of water from bodies, although each class does so in a distinct way.

High ceiling/loop diuretic:

High ceiling diuretics may cause a substantial diuresis – up to 20% of the filtered load of NaCl (salt) and water. This is large in comparison to normal renal sodium reabsorption which only about 0.4% of filtered sodium in the urine. Loop diuretics have this ability, and are therefore often synonymous with high ceiling diuretics. Loop diuretics, such as furosemide, inhibit the body's ability to reabsorb sodium at the ascending loop in the nephron, which leads to an excretion of water in the urine, whereas water normally follows sodium back into the extracellular fluid. Other examples of high ceiling loop diuretics include ethacrynic acid and torsemide.

Thiazides:

Thiazide-type diuretics such as hydrochlorothiazide act on the distal convoluted tubule and inhibit the sodium-chloride symporter leading to a retention of water in the urine, as water normally follows penetrating solutes. Frequent urination is due to the increased loss of water that has not been retained from the body as a result of a concomitant relationship with sodium loss from the convoluted tubule.

Example-

- Chlorothiazide
- Chlorthalidone

- Indapamide
- Hydrochlorothiazide.

Carbonic anhydrase inhibitors:

Carbonic anhydrase inhibitors inhibit the enzyme carbonic anhydrase which is found in the proximal convoluted tubule. This results in several effects including bicarbonate accumulation in the urine and decreased sodium absorption. Drugs in this class include acetazolamide and methazolamide.

Potassium-sparing diuretics:

These are diuretics which do not promote the secretion of potassium into the urine; thus potassium is retained and not lost as much as with other diuretics. The term "potassium-sparing" refers to an effect rather than a mechanism or location; nonetheless, the term almost always refers to two specific classes that have their effect at similar locations:

• Aldosterone antagonist: spironolactone, which is a competitive

antagonist of aldosterone. Aldosterone normally adds sodium channels in the principal cells of the collecting duct and late distal tubule of the nephron. Spironolactone prevents aldosterone from entering the principal cells, preventing sodium reabsorption. Similar agentsare eplerenone and potassium canreonate.

• Epithelial sodium channel blockers: Amiloride and Triamterene.

Calcium-sparing diuretics:

The term "calcium-sparing diuretic" is sometimes used to identify agents that result in a relatively low rate of excretion of calcium. The reduced concentration of calcium in the urine can lead to an increased rate of calcium inserum. The sparing effect on calcium can be beneficial in hypocalcemia, or unwanted in hypercalcemia.

The thiazides and potassium-sparing diuretics are considered to be calcium-sparing diuretics.

• The thiazides cause a net decrease in calcium lost in urine.

• The potassium-sparing diuretics cause a net increase in calcium lost in urine, but the increase is much smaller than the increase associated with other diuretic classes. By contrast, loop diuretics promote a significant increase in calcium excretion.

Osmotic diuretics:

Osmotic diuretics (e.g. mannitol) are substances that increase osmolality but have limited tubular epithelial cell permeability. They work primarily by expanding extracellular fluid and plasma volume, therefore increasing blood flow to the kidney, particularly the peritubular capillaries. This reduces medullary osmolality and thus impairs the concentration of urine in the loop of Henle (which usually uses the high osmotic and solute gradient to transport solutes and water).

Furthermore, the limited tubular epithelial cell permeability increases osmolality and thus water retention in the filtrate. It was previously believed that the primary mechanism of osmotic diuretics such as mannitol is that they are filtered in the glomerulus, but cannot be reabsorbed. Thus their presence leads to an increase in the osmolarity of the filtrate and to maintain osmotic balance, water is retained in the

urine.

Example-

- Glycerin (Glycerol)
- Isosorbide
- Mannitol IV

Good control of blood glucose level

This will help to delay the progression of the kidney disease and to reduce risk of developing associated cardiovascular diseases, such as heart disease and stroke. Ideally, the aim is to maintain HbA1c less than 48 mmol/mol but this may not always be possible to achieve and the target level of HbA1c should be agreed on an individual basis between patient and doctor.

Good control of blood pressure

Strict blood pressure control is likely to reduce the risk of developing cardiovascular diseases and prevent or delay the progression of kidney disease. Most people should already be taking an ACE inhibitor or AIIRA (described above). These drugs lower blood pressure. However, if blood pressure remains at 130/80 mm Hg or more than one or more additional drugs may be advised to lower blood pressure to below this level.

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2.1 Aim and Objectives:

Chronic Kidney Disease & Diabetes Mellitus are closely associated with each other. Many people developed Chronic Kidney Disease due to their long time sufferings form Diabetes Mellitus. We want to survey this prevalence of two diseases among the population of Dhaka City. This survey was conducted at Rampura branch and Jurain branch of BIRDEM, the Bangladesh Institute of Research and Rehabilitation for Diabetes, under National Health Care Network. Almost 144 patients with Diabetes Mellitus were interviewed to find out their association with chronic kidney disease.

The main objectives of this study were-

- To evaluate the association of chronic kidney disease with Diabetes Mellitus (DM).
- To identify the risk factors associated with Diabetes Mellitus & Chronic Kidney Disease.
- To find out the frequency of doctor visits regarding Diabetes Mellitus & Chronic Kidney Disease among the patients.
- To evaluate the treatment pattern of Diabetes Mellitus & Chronic Kidney Disease.
- To figure out the range of HbA1C level among the patients of Diabetes Mellitus.
- To determine the creatinine level among the patients of Chronic Kidney Disease.
- To establish some correlations between risk factors and the presence of Chronic Kidney Disease.

3.1 Literature Review:

Chronic kidney disease (CKD) is common and can be found in up to 23% of patients with diabetes. The recommended hemoglobin A1c goal for these patients is also < 7.0%. Medication therapy for diabetes may require dose adjustments or may be contraindicated in patients with CKD. Chronic kidney disease (CKD) is a common condition that is estimated to affect 11% of the U.S. population, or 19 million people, and over 50 million people worldwide. Similarly, diabetes is of an epidemic scale, with prevalence estimates of 20 million people in the United States and 171 million people worldwide. Diabetes is often associated with CKD and for 45% of patients who receive dialysis therapy, diabetes is the primary cause of their kidney failure.4Additionally, moderate to severe CKD is estimated to be found in 15-23% of patients with diabetes (Cavanaugh, 2007)

Brancati et al. suggested that Diabetes mellitus is a strong independent risk factor for end-stage renal disease (ESRD). Over an average follow-up of 16 years, there were 136 cases of ESRD in 5147 diabetic men and 678 cases in 327 397 nondiabetic men. Age-adjusted incidence of all-cause ESRD in the diabetic men was 199.8 per 100 000 person-years compared with 13.7 per 100 000 person years in their nondiabetic counterparts (Brancati et al., 1997).

Chronic kidney disease (CKD) is a worldwide health alarm that is rising for the most part of the world as the result of increasing incidences of diabetes, hypertension and other cardiovascular diseases. Ginawi et al. studied about the risk factors for CKD in Hail region, KSA. They found high percentages of risk factors were indicated in a family history (FH) of DM representing 72%, followed by family history of hypertension, recurrent urinary tract infection, DM, family history of renal disease, hypertension, and analgesic abuse, constituting 65%, 59%, 26%, 26%, 25%, and 22% respectively (Ginawi et al., 2013).

Coresh et al serum conducted creatinine assay provide a basis for estimating the prevalence and distribution of chronic kidney disease (CKD) in the United States using standardized criteria based on estimated glomerular filtration rate (GFR) and persistent albuminuria. The prevalence of CKD in the US adult population was 11% (19.2 million). By stage, an estimated 5.9 million individuals (3.3%) had stage 1 (persistent albuminuria with a normal GFR), 5.3 million (3.0%) had stage 2 (persistent albuminuria with a GFR of 60 to 89 mL/min/1.73 m2), 7.6 million (4.3%)

had stage 3 (GFR, 30 to 59 mL/min/1.73 m2), 400,000 individuals (0.2%) had stage 4 (GFR, 15 to 29 mL/min/1.73 m2), and 300,000 individuals (0.2%) had stage 5, or kidney failure. Aside from hypertension and diabetes, age is a key predictor of CKD, and 11% of individuals older than 65 years without hypertension or diabetes had stage 3 or worse CKD (Coresh et al., 2003).

Meer et al. survey to assess the prevalence and severity of CKD in patients with diabetes and hypertension; and identify whether age, sex, diabetes, and hypertension are associated with CKD. They found the prevalence of CKD was 28% in diabetes and 21% in hypertension. They suggested that in primary care, more than one-quarter of patients with diabetes and about one-fifth of patients with hypertension have CKD. The high prevalence justifies longitudinal follow-up in order to evaluate whether intensified cardiovascular risk management is beneficial in this primary care population (Meer et al., 2010).

Afkarian et al. examined 10-year cumulative mortality by diabetes and kidney disease status for 15,046 participants. Type 2 diabetes associates with increased risk of mortality, but how kidney disease contributes to this mortality risk among individuals with type 2 diabetes is not completely understood. Here, we examined 10-year cumulative mortality by diabetes and kidney disease status for 15,046 participants in the Third National Health and Nutrition Examination Survey (NHANES III) by linking baseline data from NHANES III with the National Death Index. Kidney disease, defined as urinary albumin/creatinine ratio ≥ 30 mg/g and/or estimated GFR ≤60 ml/min per 1.73 m2, was present in 9.4% and 42.3% of individuals without and with type 2 diabetes, respectively. Among people without diabetes or kidney disease (reference group), 10-year cumulative all-cause mortality was 7.7% (95% confidence interval [95% CI], 7.0%–8.3%), standardized to population age, sex, and race. Among individuals with diabetes but without kidney disease, standardized mortality was 11.5% (95% CI, 7.9%-15.2%), representing an absolute risk difference with the reference group of 3.9% (95% CI, 0.1%-7.7%), adjusted for demographics, and 3.4% (95% CI, -0.3% to 7.0%) when further adjusted for smoking, BP, and cholesterol. Among individuals with both diabetes and kidney disease, standardized mortality was 31.1% (95% CI, 24.7%-37.5%), representing an absolute risk difference with the reference group of 23.4% (95% CI, 17.0%–29.9%), adjusted for demographics, and 23.4% (95% CI, 17.2%–29.6%) when further adjusted. We observed similar patterns for cardiovascular and

noncardiovascular mortality. In conclusion, those with kidney disease predominantly account for the increased mortality observed in type 2 diabetes (Afkarian et al., 2013).

Giuseppe et al. evaluated the rate and determinants of concordance between advanced diabetic retinopathy (DR) and chronic kidney disease (CKD), as assessed by both albuminuria and estimated glomerular filtration rate (eGFR), in the large cohort of the Renal Insufficiency And Cardiovascular Events (RIACE) Italian multicenter study. They found CKD was present in 58.64% of subjects with advanced DR, whereas advanced DR was detectable only in 15.28% of individuals with any CKD and correlated with the albuminuric CKD phenotypes more than with the nonalbuminuric phenotype. Age, male sex, diabetes duration, hemoglobin A1c, hypertension, triglycerides, previous cardiovascular disease, and, inversely, HDL-cholesterol correlated independently with the presence of any CKD in individuals with advanced DR; correlates differed according to the presence of albuminuria, reduced eGFR, or both. Conversely, factors associated with the presence of advanced DR in subjects with any CKD were diabetes treatment, previous cardiovascular disease, albuminuria, and, inversely, smoking, eGFR, and age at diagnosis (Giuseppe et al., 2012).

4.1 Materials and Method:

Present study protocol:

- 1. Number of study center : 02
- 2. Number of patients : 144
- 3. Site of study : 2

Study center 1: NHN Rampura Centre, West Rampua, Dhaka-1219.

Study center 2: NHN Jurain Centre, Jurain, Dhaka-1236.

4. Duration of study: 6 months

Inclusive criteria

In this cross sectional study, medical records of patients of chronic kidney disease with diabetes mellitus in two branches of Birdem hospital were studied during the time period. Demographic data, clinical method, treatment pattern and related complications were extracted from the patient's medical files or diabetic book. In some patients diagonosis of diabetes and kidney disease was recorded in their medical files and they were on glucose lowering agents, diuretic agent etc. About 150 patient's information data was collected for this research work. In this study, branches of Birdem hospital was preferred because a good number of diabetes patients visit here, many of them suffering with chronic kidney disease and they are affected with diabetes mellitus for a long time. The research data was collected by interviewing individual patients and the researcher directly communicated with the patients by questioning the patient as per the following questionnaire.

| Data Collection Form 1. Name- 2. Sex - Image: Female 3. Age - Image: 20 Image: 20-44 Image: Sex - Image: 20 Image: 20-44 Image: Sex - Image: 20 Image: 20-44 Image: Sex - Image: 20-44 Image: 20-45 | | | | | |
|---|--|--|--|--|--|
| 2. Sex - Female Male | | | | | |
| | | | | | |
| 3. Age | | | | | |
| | | | | | |
| 4. Weight- | | | | | |
| 5. Impression about social class | | | | | |
| Rich Upper middle Poor | | | | | |
| 6. Area of residence- Rural Urban S-urban | | | | | |
| 7. How long you are diagonosed with Diabetes Mellitus? | | | | | |
| < 1 year 1-3 years 3-5 years 5-10 years > 10 years | | | | | |
| 8. Family history of Diabetes Mellitus? | | | | | |
| Yes No | | | | | |
| 9. Blood pressure- Yes No | | | | | |
| 10. Treatment of Diabetes Mellitus- | | | | | |
| Insulin only Oral medication Both | | | | | |
| 11. An insulin shot- 🗖 1 or 2 times a day 🗖 3 or more times a day | | | | | |
| Oral Medication | | | | | |
| 12. How often did you take your diabetes medication since your last visit? | | | | | |
| Always Usually Sometimes Rarely Never | | | | | |
| 13. Plasma glucose level-Fasting:Random: | | | | | |
| 14. How many times you visit a doctor in a year? | | | | | |
| times. | | | | | |
| 15. Smoking habit Bettle leaf | | | | | |
| | | | | | |
| 16. Stage of kidney problem- | | | | | |
| AKF CKD ESRD | | | | | |
| | | | | | |
| 19. How long has it been since you were first diagnosed? | | | | | |
| \square < 1 year \square 1-3 years \square 3-5 years \square 5-10 years \square > 10 year | | | | | |

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20.How was this diagnosed? (Check those that apply)

Blood test (elevated creatinine)

Protein(albumin) in the urine

Other:

21. Have you been told what caused your kidney disease(risk factors)?

| Diabetes, |
|--|
| High blood pressure, |
| Glomerulonephritis |
| kidney stones |
| Analgesic abuse, |
| Herbal use |
| Smoking |
| Stroke |
| Heart attack |
| |
| 22. Have you ever had any of the following (Check if yes): |
| Kidney problems at birth or in childhood? |
| Hospitalization due to kidney failure? |
| Kidney failure while hospitalized for another reason? |
| Kidney stones? |
| Bladder or kidney infections? |
| Difficulty emptying your bladder? |
| Bladder or other urologic surgery? |
| Radiation to the abdomen or pelvis? |
| Chemotherapy for cancer? |
| ☐ Family history of kidney disease? |
| Blood in the urine? |
| Foamy urine? |
| 24. HbA1C: $\square < 7 \square \ge 7$ |
| 25. Creatinine: |

5.1Result:

From the survey conducted, there are some findings which may have vital implication which proves the fact that there is some link between chronic kidney disease & diabetes mellitus. Major findings are shown here as per the following:

5.1.1 Gender Distribution:

Table 5.1.1: Gender distribution among survey populations

| Gender | No. | Prevalence (%) |
|--------|-----|----------------|
| Female | 86 | 59.72 |
| Male | 58 | 40.28 |

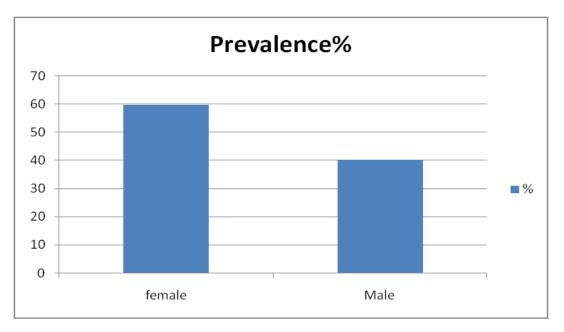


Figure 5.1.1: Gender distribution

From the Figure 5.1.1 and Table 5.1.1, it is observed that, majority of the survey population were female which contributes around 60% of the population.

5.1.2 Age Distribution:

Table 5.1.2: Age distribution of patients

| Age Range | Number of cases out of 144 | Prevalence (%) |
|-----------|----------------------------|----------------|
| | samples | |
| <20 | 0 | 0 |
| 22-40 | 29 | 20.13 |
| 45-64 | 82 | 56.95 |
| >65 | 33 | 22.92 |

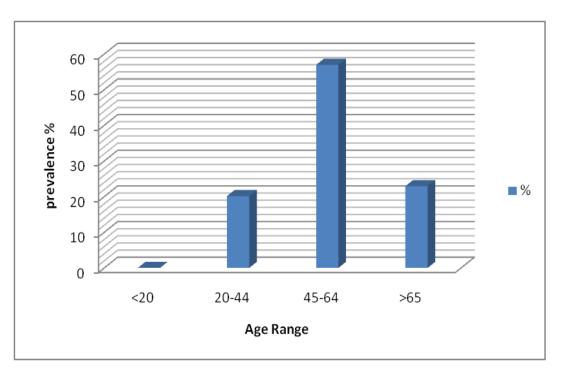


Figure 5.1.2: Age distribution of patient.

Here we observed that, patients aged from 45 to 64, highly suffers from diabetes mellitus and the prevalence is around 57%. The second highest group of patients was aged above 54, where the prevalence is around 23% and 29% patient group came from the age above 65.

5.1.3 Socio-economical condition:

| Total Sample | Socio-economical | Number of Patients | Prevalence (%) |
|--------------|--------------------|--------------------|----------------|
| | Status | Suffering | |
| | Upper-Middle class | 41 | 28.47 |
| 144 | Middle class | 83 | 57.64 |
| | Poor | 19 | 13.2 |

Table 5.1.3: Socio-economical condition of diabetes mellitus patients

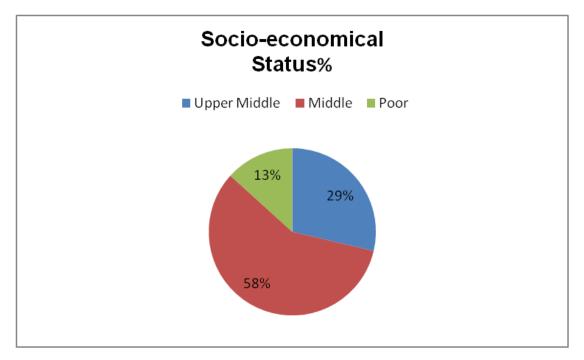


Figure 5.1.3: Socio-economical condition of diabetes mellitus patients.

In case of socio-economical condition of diabetes mellitus, it is observed in Figure 5.1.3 and Table 5.1.3 that 58% patients were from middle class, 29% people were from upper-middle class, and 13% were from poor economical status out of 144 samples.

5.1.4 Prevalence of chronic kidney disease with diabetes mellitus:

Table 5.1.4: Prevalence of patients of chronic kidney disease with diabetes mellitus

| Affecting Period of DM | Number of Patient | Prevalence of Chronic Kidney |
|------------------------|-------------------|------------------------------|
| (Year) | | Disease with DM |
| <1 | 1 | 0.7 |
| 1-3 | 14 | 9.72 |
| 3-5 | 26 | 18.06 |
| 5-10 | 21 | 14.58 |
| >10 | 11 | 7.64 |

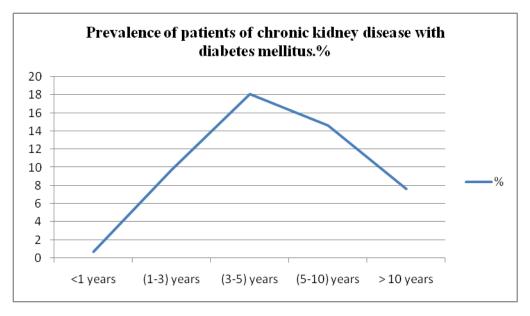


Figure 5.1.4: Prevalence of patients of chronic kidney disease with diabetes mellitus.

From Figure 5.1.4 and Table 5.1.4, it is observed that, among 73 type 2 diabetic mellitus patient who are suffering from chronic kidney disease, highest population belongs to (3-5) years and (5-10) years range which are 18.1% and 14.5% respectively. So people who are suffering from diabetic mellitus for 5 or more years have the highest chance of developing chronic kidney disease.

5.1.5 Possible causes or risk factors for chronic kidney disease:

Table 5.1.5: Risk factors that causes people kidney disease

| Risk Factors | No. of Patient | Prevalance(%) |
|------------------------------|----------------|---------------|
| Diabetes | 35 | 47.95 |
| High Blood Pressure | 27 | 36.99 |
| Kidney Stones | 6 | 8.22 |
| Analgesics Abuses | 26 | 35.62 |
| Smoking | 15 | 20.55 |
| Urinary Tract Infection(UTI) | 4 | 5.48 |

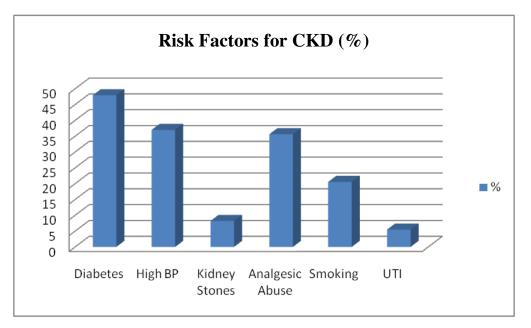


Fig 5.1.5: Risk factors that causes people kidney disease

Among 144 type 2 diabetes mellitus patients 73 of them have chronic kidney disease. Factors doctor found as the possible causes for kidney diseases are diabetes, high blood pressure, kidney stones, analgesic abuse, smoking, urinary tract infection. From Figure 5.1.5 and Table 5.1.5, it is

observed that for 48% patient suffering from kidney disease, diabetes mellitus is found as the risk factor.

5.1.6 Treatment pattern of Diabetic Patients:

Table 5.1.6: Treatment pattern of diabetes patients

| Total Sample | Drug Type | Number of Patients | Prevalence (%) |
|--------------|-----------------|--------------------|----------------|
| | Insulin | 42 | 29.17 |
| 144 | Oral Medication | 54 | 37.5 |
| | Both | 48 | 33.33 |

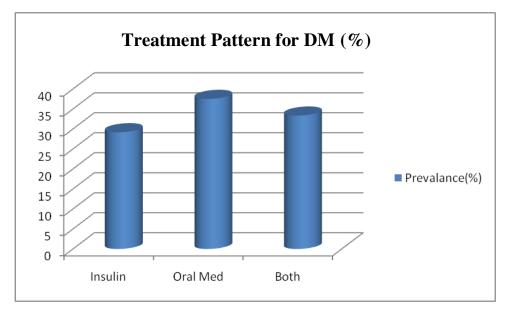


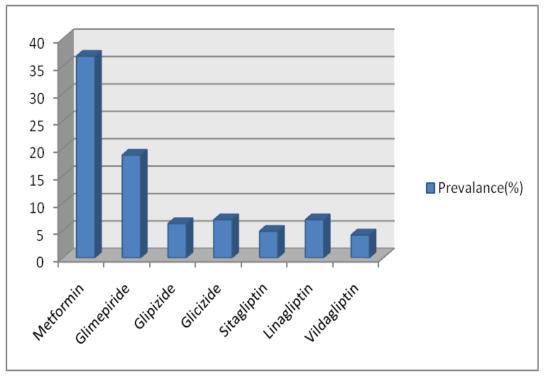
Fig 5.6.1: Treatment pattern of diabetes patients.

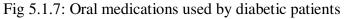
From Figure 5.1.6 and Table 5.1.6, it is seen that, in case of Type 2 diabetes mellitus about 29% patients use only insulin, 37.5% patients use oral medication and 33.33% patients use both insulin and oral medications.

5.1.7 Oral medications used by diabetic patients

Table 5.1.7: Oral medications used by diabetic patients

| Total Sample | Name of Drugs | Number of Patients | Prevalence (%) |
|--------------|---------------|--------------------|----------------|
| | Metformin | 53 | 36.81 |
| 144 | Glimepiride | 27 | 18.75 |
| 144 | Glipizide | 9 | 6.25 |
| | Gliclazide | 10 | 6.95 |
| | Sitagliptin | 7 | 4.86 |
| | Linagliptin | 10 | 6.95 |
| | Vildagliptin | 6 | 4.17 |





From Figure 5.1.7 and Table 5.1.7, it is seen that, in case of Type 2 diabetes mellitus about 36.8% patients use Metformin, as oral hypoglycemic drug, 18.75% patients use Glimepiride. Apart from these two glipizide, gliclazide, sitagliptin, linagliptin, vildagliptin etc are commonly used.

5.1.8 Diagnostic tools for CKD:

Table 5.1.8: Diagnostic tools for CKD

| Total | Diagnostic tool | No. of patient | Prevalence (%) |
|-------|-------------------------|----------------|----------------|
| | Blood (creatinine) Test | 100 | 69.5 |
| 144 | Protien in urine | 70 | 48.6 |
| | Other | 0 | 0 |

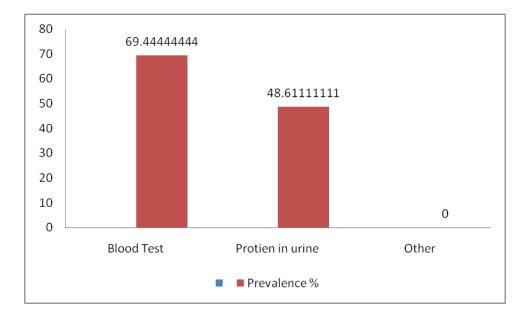


Fig 5.1.8: Diagnostic tools for CKD

From table and fig. 5..1.8 it is seen that 69.5% patient was given blood test and 48.6% people were given urine test.

5.1.9 HbA1C range of diabetic patients:

HbA1c refers to glycated haemoglobin, which identifies average plasma glucose concentration. Table 5.1.9: HbA1C range of diabetic patients

| Total Sample | HbA1C Range (%) | Number of Patients | Prevalence (%) |
|--------------|-----------------|--------------------|----------------|
| | < 7 | 60 | 41.67 |
| 144 | 7-9 | 69 | 47.92 |
| | 10-14 | 8 | 5.56 |
| | >14 | 7 | 4.86 |

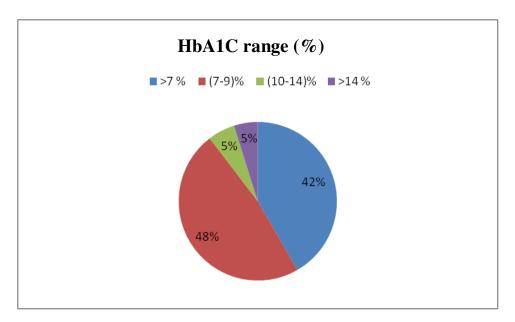


Fig 5.1.9: HbA1C range of diabetic patients

From Figure 5.1.9 and Table 5.1.9, it is seen that majority of the patient (48%) had the HbA1C level in between 7% to 9%. Secondly, 42% patient had their HbA1C level in below 7%. And 5% patient had the HbA1C level in between 10% to 14% and the remaining 5% had above 14%.

5.1.10 Creatinine range:

Table 5.1.10: Creatinine range

| Total Sample | Creatinine Range | Number of | Prevalence (%) |
|--------------|------------------|-----------|----------------|
| | (ml/dl) | Patients | |
| | 0.5-0.9 | 41 | 28.47 |
| 144 | 1-1.5 | 42 | 29.17 |
| | 1.6-2.5 | 47 | 32.64 |
| | 2.6-3.5 | 12 | 8.33 |
| | 3.6-4.5 | 2 | 1.39 |

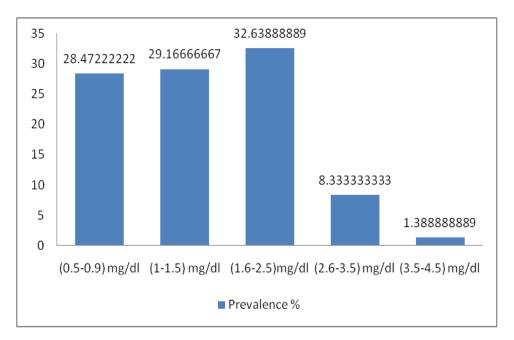


Fig 5.1.10: Creatinine range

From Figure 5.1.10and Table 5.9, it is seen that 32.6% patients had the creatinine range in between (1.6-2.5) ml\dl. Secondly, 29% patients Creatinine range in between (1-1.5) ml\dl and 28.5% patients creatinine range in between (0.5-0.9) ml\dl.

5.2 Discussion:

Diabetic is becoming the leading cause of chronic kidney disease (CKD) and kidney failure in Bangladesh. Diabetes is a disease that affects the body's ability to produce or use insulin. When the body turns the food eaten into energy (also called sugar or glucose), insulin is used to move this sugar into the cells. If someone produces little or no insulin, or if the body cannot use the insulin (insulin resistant), the sugar remains in the bloodstream instead of going into the cells. Over time, high levels of sugar in the blood damage tiny blood vessels throughout the body including the filters of the kidneys.

The study was performed on 144 populations and in rural area. Among them about 60% was female and 40% was male. Among them majority people has age range (45-64) which accounts for about 57% of the population, 20% were between (20-44) age range, 23% were more than 65 years old and no one was found below 20 years. So, it has been seen that with the increase in age association of CKD with diabetes increased. At the same time it has been seen that prevalence of CKD with diabetes mellitus was also increased with the affecting period of diabetes mellitus. People suffering from diabetes for 3 or more years are prone to develop CKD. 18% has affecting years between (3-5) years, 14.5% has between (5-10) years, 7.6% has more than 10 years and few have affecting years less than 3 years.

Among 144 type 2 diabetes mellitus patients 73 of them have chronic kidney disease. Factors doctor found as the possible causes for kidney diseases are diabetes, high blood pressure, kidney stones, analgesic abuse, smoking, urinary tract infection. It is observed that for 48% patient suffering from kidney disease, diabetes mellitus is found as the risk factor, high blood pressure is found for 37% patient, analgesic abuse for 36.5% and other risk factors present in patients is found in little amount.

While estimating socio economic class it is found that majority people are belong to middle class which is 58%. So it can be said that this class patient are at more risk to develop CKD while suffering diabetes mellitus.

In case of Type 2 diabetes mellitus about 29% patients use only insulin, 37.5% patients use oral medication and 33.33% patients use both insulin and oral medications. And in case of Type 2 diabetes mellitus about 36.8% patients use Metformin, as oral hypoglycemic drug, 18.75%

Association of Chronic kidney disease with Diabetes mellitus: A survey on its prevalence, treatment pattern and risk factors in context of Bangladesh

patients use Glimepiride. Apart from these two glipizide, gliclazide, sitagliptin, linagliptin, vildagliptin etc are commonly used.

People having CKD with diabetes mellitus usually have HbA1C level more than 7. In this study 48% population have HbA1C range between (7-9)%, 5.5% between (10-14)%, 42% patient had their HbA1C level in below 7% and remaining 5% had above 14%.

Also, it is seen that 32.6% patients had the creatinine range in between (1.6-2.5) ml\dl. Secondly, 29% patients Creatinine range in between (1-1.5) ml\dl and 28.5% patients creatinine range in between (0.5-0.9) ml\dl. So, high creatinine in blood is a symptom of kidney diseases.

Usually GFR (glomerular filtration rate) level test is considered as standard and reliable diagnostic tool for CKD. But in our country creatinine level test is usually used. In this study 69.5% patient was given blood test and 48.6% people were given urine test.

6.1 Conclusion:

Diabetes mellitus poses a serious threat to developing countries like Bangladesh as it associates with the development of chronic kidney disease. Chronic kidney disease and diabetes are becoming common diseases that affect a large proportion of the population in Bangladesh. This survey work reflects the overall figure of age group, gender distribution, weight variation, socio-economical condition, creatinine range, HbA1C range, related complications and progressive status of diabetic & chronic kidney patients in Dhaka city.

The management of patients with diabetes and chronic kidney disease necessitates attention to several aspects of care. Depending on the severity of the CKD, drug regimens, including those for glycemic control, and dietary intake may require adjustments. Also a disciplined life style, change in food habit, regular physical exercise, sufficient pure water intake, control body weight and enjoying life without any stress concurrently help the patients to manage this chronic disease at a large scale and provide a long live healthy life.

Screening for development of nephropathy should be performed on a regular basis to identify microalbuminuria or reductions in GFR and if identified, the diabetes regimen should be tailored accordingly. Multidisciplinary care, including teamwork among physicians, nurses, pharmacists, dietitians, and social workers, may provide the optimal system for maximizing the care of complex chronic disease patients. Importantly, glycemic control should be optimized for the patient, attaining the necessary control to reduce complications but done in a safe, monitored manner.

References:

Afkarian, M., Sachs, M.C., Kestenbaum, B., Hirsch, I.B., Tuttle, K.R., Himmelfarb, J. and de Boer, I.H. (2013) 'Kidney disease and increased mortality risk in type 2 diabetes', Journal of the American Society of Nephrology, 24(2), pp. 302–308.

American Diabetes Association (2004) 'Diagnosis and classification of diabetes Mellitus', Position Statements, 27(suppl 1), pp. 10–5.

Andrassy, K.M. (2013) 'Comments on 'KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease'', *Kidney International*, 84(3), pp. 622–623.

Belleza, M. (2016) *Chronic renal failure nursing care and management: Study guide*. Available at: http://nurseslabs.com/chronic-renal-failure/ (Accessed: 12 November 2016).

Brancati, F.L., Whelton, P.K., Randall, B.L., Neaton, J.D., Stamler, J. and Klag, M.J. (1997) 'Risk of end-stage renal disease in diabetes Mellitus', JAMA, 278(23), pp. 2069–2074.

Cavanaugh, K.L. (2007) 'Diabetes management issues for patients with chronic kidney disease', *Clinical Diabetes*, 25(3), pp. 90–97.

Cleveland Clinic (1995) What is diabetes Mellitus: Symptoms & treatment. Available at: http://my.clevelandclinic.org/health/diseases_conditions/hic_Diabetes_Basics/hic_Diabetes_Mell itus_An_Overview (Accessed: 30 October 2016).

Cleveland Clinic (2000) Diabetes Mellitus treatment. Available at: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/endocrinology/diabetes -mellitus-treatment/ (Accessed: 8 November 2016).

Coresh, J., Astor, B.C., Greene, T., Eknoyan, G. and Levey, A.S. (2003) 'Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third national health and nutrition examination survey', American Journal of Kidney Diseases, 41(1), pp. 1–12.

Drugs.com (2000) List of Antidiabetic agents. Available at: https://www.drugs.com/drugclass/antidiabetic-agents.html (Accessed: 10 June 2016).

Drugs.com (2000) *List of diuretics*. Available at: https://www.drugs.com/drugclass/diuretics.html (Accessed: 10 June 2016).

Elsevier (2016) Williams textbook of Endocrinology. Available at: https://www.elsevier.com/books/williams-textbook-of-endocrinology/melmed/978-1-4377-0324-5 (Accessed: 30 October 2016).

Ginawi, Abdelmajeed, I., Gadelkarim, H.G., Ashankyty, I.M., Altamimi, T., Almogbel, M., Alsuedaa, A., Akbar, D., Albeladi, F., Alrashdan, A., Jastaniah, S.D. (2013) 'SURVEY FOR POTENTIAL RISK FACTORS FOR SUSCEPTIBILITY TO CHRONIC KIDNEY DISEASE IN HAIL REGION, KSA', Management in Health, 17(2).

Häggström, M. (2012) Type 2 diabetes. Available at: http://conditions.healthgrove.com/l/1057/Type-2-Diabetes (Accessed: 12 November 2016).

Healthwise (1995) *Stages of chronic kidney disease-topic overview*. Available at: http://www.webmd.com/a-to-z-guides/tc/stages-of-chronic-kidney-disease-topic-overview (Accessed: 12 November 2016).

Meer, V., Wielders, H.P.M., Grootendorst, D.C., de Kanter, J.S., Sijpkens, Y.W., Assendelft, W.J., Gussekloo, J., Dekker, F.W. and Groeneveld, Y. (2010) 'Chronic kidney disease in patients with diabetes mellitus type 2 or hypertension in general practice', *British Journal of General Practice*, 60(581), pp. 884–890.

Melmed, S., Polonsky, K.S., Larsen, R.P., Kronenberg, H.M., Franco, K.L. and Garcia-Prada, H. (2011) *Williams textbook of Endocrinology: Expert consult-online and print*. 12th edn. Philadelphia: Elsevier Health Sciences.

National institute of diabetes and digestive and kidney diseases (2014), Causes of Diabetes, Available at: https://www.niddk.nih.gov/health-information/diabetes/causes (Accessed: 8 November 2016). National Kidney Foundation (2016) *About chronic kidney disease*. Available at: https://www.kidney.org/kidneydisease/aboutckd (Accessed: 12 November 2016).

Sattar, N., Preiss, D., Murray, H.M., Welsh, P., Buckley, B.M., de Craen, A.J., Seshasai, S.R.K.,
McMurray, J.J., Freeman, D.J., Jukema, J.W., Macfarlane, P.W., Packard, C.J., Stott, D.J.,
Westendorp, R.G., Shepherd, J., Davis, B.R., Pressel, S.L., Marchioli, R., Marfisi, R.M.,
Maggioni, A.P., Tavazzi, L., Tognoni, G., Kjekshus, J., Pedersen, T.R., Cook, T.J., Gotto, A.M.,
Clearfield, M.B., Downs, J.R., Nakamura, H., Ohashi, Y., Mizuno, K., Ray, K.K. and Ford, I.
(2010) 'Statins and risk of incident diabetes: A collaborative meta-analysis of randomised statin
trials', *The Lancet*, 375(9716), pp. 735–742. doi: 10.1016/s0140-6736(09)61965-6.

WHO (2010) Diabetes mellitus. Available at: http://www.who.int/mediacentre/factsheets/fs138/en/ (Accessed: 30 October 2016).

WHO (2016) *Estimates for 2000–2012*. Available at:

http://www.who.int/healthinfo/global_burden_disease/estimates/en/index1.html (Accessed: 17 July 2016).

WHO (2016) *Diabetes*. Available at: http://www.who.int/mediacentre/factsheets/fs312/en/ (Accessed: 5 July 2016).

Uhlig, K., Berns, J.S., Kestenbaum, B., Kumar, R., Leonard, M.B., Martin, K.J., Sprague, S.M. and Goldfarb, S. (2010) 'KDOQI US commentary on the 2009 KDIGO clinical practice guideline for the diagnosis, evaluation, and treatment of CKD–Mineral and bone disorder (CKD-MBD)', American Journal of Kidney Diseases, 55(5), pp. 773–799.