A survey on Practice and Treatment towards Diabetes mellitus of diabetic patients in Bangladesh perspective

A dissertation submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy.

Supervised by

Faculty of Department of pharmacy

Nafisa Tanjia

Lecturer

Department of Pharmacy

Submitted By

Safia Sultana

ID: 2011-1-78-001

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DEDICATION

This Research Paper Is Dedicated

To My Beloved Parents, Who Are My biggest inspiration …

Declaration by the Research Candidate

I, Safia Sultana, hereby declare that this dissertation, entitled **"A survey on Practice and Treatment towards Diabetes mellitus of diabetic patients in Bangladesh perspective'"** submitted to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Honors) is a genuine & authentic research work carried out by me. The contents of this dissertation, in full or in parts, have not been submitted to any other institute or University for the award of any degree or Diploma of Fellowship.

Signature of the Candidate

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ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation, entitled **"A survey on Practice and treatment towards Diabetes mellitus of diabetic patients in Bangladesh perspective"** is a bona fide research work done by Safia Sultana (ID: 2011-1-78-001), in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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Dr. Chowdhury Faiz Hossain

Professor & Chairperson

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Aftabnagar, Dhaka.

CERTIFICATION BY THE SUPERVISOR

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ABSTRACT

Diabetes mellitus is a rapidly growing disease around the world., About 387 million people have diabetes worldwide. This is equal to 8.3% of the adult population, with equal rates in both women and men. In the years 2012 to 2014, diabetes is estimated to have resulted in 1.5 to 4.9 million deaths per year. In Bangladesh, the number diabetic patient has also increased due to lack of in appropriate practice and treatment. There is little work done on diabetes mellitus as well as practice and treatment towards Diabetes mellitus of diabetic patients in Bangladesh. The main objective of our study was to see the recent consequences of practice and treatment pattern of Diabetes mellitus. It was a survey based study and performed on 202 diabetic patients in BIRDEM (Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders) at Shahbag, Dhaka, BIRDEM at Rampura, Dhaka and Sangshad Vaban park. In this study 51.44% male and 48.55% female participants were found. Patients were selected randomly. Here common factors are considered affecting diabetes practice and treatment pattern were sex, age, level of education, marital status, profession, and income, mode of diagnosis and duration of diabetes. Only Diabetic patients were selected as study population. 96.53% of them were married and 3.96% were single. The study also showed that the maximum percentage (20.79%) of normal range of fasting blood glucose level was 4.1-6 mg/ml and the maximum percentage (33.66%) normal range of random blood glucose level was 8.1-12mg/ml. HbA1c test which is very essential for the measurement of diabetes is not very popular among the patients. Only small amount of about 13.86% performed this test and remaining 86.14% don't heard about this test. Our study also showed that people in Bangladesh frequency of visiting healthcare provider has risen alarmingly, 71.78% patients visit healthcare provider more than twice in a year, 22.77% visit twice in a year and the patient also concern about controlling their diabetes .In this regard we saw that 27.54% people inject insulin and 22.72% take medicine 25.4% taking exercise 20.32% took healthy diet to manage hyperglycemic condition. We found that people are more cautious about their diabetic condition and their treatment pattern. They know the sign and symptoms and management practice of diabetes in hyperglycemic and hypoglycemic condition. In spite of that Government & society should take proper and powerful steps to decrease the number of diabetic patients by creating awareness among mass population.

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1.1 Overview

The term diabetes mellitus describes a metabolic disorder and characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs. Diabetes mellitus may present with characteristic symptoms such as thirst, polyuria, blurring of vision, and weight loss. In its most severe forms, ketoacidosis or a non-ketotic hyperosmolar state may develop and lead to stupor, coma and, in absence of effective treatment, death. Often symptoms are not severe, or may be absent, and consequently hyperglycemia sufficient to cause pathological and functional changes may be present for a long time before the diagnosis is made. The long-term effects of diabetes mellitus include progressive development of the specific complications of retinopathy with potential blindness, nephropathy that may lead to renal failure, and/or neuropathy with risk of foot ulcers, amputation, Charcot joints, and features of autonomic dysfunction, including sexual dysfunction. People with diabetes are at increased risk of cardiovascular, peripheral vascular and cerebrovascular disease. Several pathogenetic processes are involved in the development of diabetes. These include processes which destroy the beta cells of the pancreas with consequent insulin deficiency, and others that result in resistance to insulin action. The abnormalities of carbohydrate, fat and protein metabolism are due to deficient action of insulin on target tissues resulting from insensitivity or lack of insulin (World Health Organization 1999, Department of Non communicable Disease Surveillance, Geneva).

1.2 Impact of diabetes

Over time, diabetes can lead to blindness, kidney failure, and nerve damage. These types of damage are the result of damage to small vessels, referred to as micro vascular disease. Diabetes is also an important factor in accelerating the hardening and narrowing of the arteries (atherosclerosis), leading to strokes, coronary heart disease, and other large blood vessel diseases. This is referred to as macro vascular disease. Diabetes affects approximately 26 million people in the United States, while another 79 million have prediabetes. An estimated 7 million people in the United States have diabetes and don't even know it.From an economic perspective, the total annual cost of diabetes in 2012 was estimated to be 245 billion dollars in the United States. This included 116 billion in direct medical costs (healthcare costs) for people with diabetes and another 69 billion in other costs due to

disability, premature death, or work loss. Medical expenses for people with diabetes are over two times higher than those for people who do not have diabetes. These numbers reflect only the population in the United States. Globally, the statistics are staggering. Diabetes was the 7th leading cause of death in the United States listed on death certificates in 2007 (MedicineNet.com 2014).

1.3 How insulin works

Insulin is a vital hormone produced by cells in pancreas. Insulin works to move glucose from the blood and into cells for energy or storage for later energy. During digestion, foods that contain carbohydrates are digested and converted to glucose. This causes a rise in blood glucose. The increase in sugar signals pancreas to produce the amount of insulin needed to manage the level of sugar in your blood. When insulin is produced, glucagon is suppressed. Insulin stimulates the cells throughout the body to take in glucose from bloodstream. Cells then use glucose as energy.In order to help fuel the body between meals, excess glucose is stored in cells of the liver and muscles as glycogen. As glucose is converted to energy or stored in the liver and muscles, its levels in blood are reduced (Susan York Morris 2014).

1.4 Role of glucagon

Glucagon is a hormone that is produced by alpha cells in a part of pancreas known as islets of langerhans. Glucagon plays an active role to regulate the utilization of glucose or fats. Glucose is released in response to low blood glucose levels and events whereby the body needs additional glucose such as in response to vigorous exercise.

When glucagon released it can perform following tasks:

- Stimulating liver to break down glycogen to be released into blood as glucose.
- Activating gluconeogenesis, conversion of amino acid into glucose.
- Breaking down stored fat (triglycerides) into fatty acid for use as fuel by cells. (diabetes.co.uk)

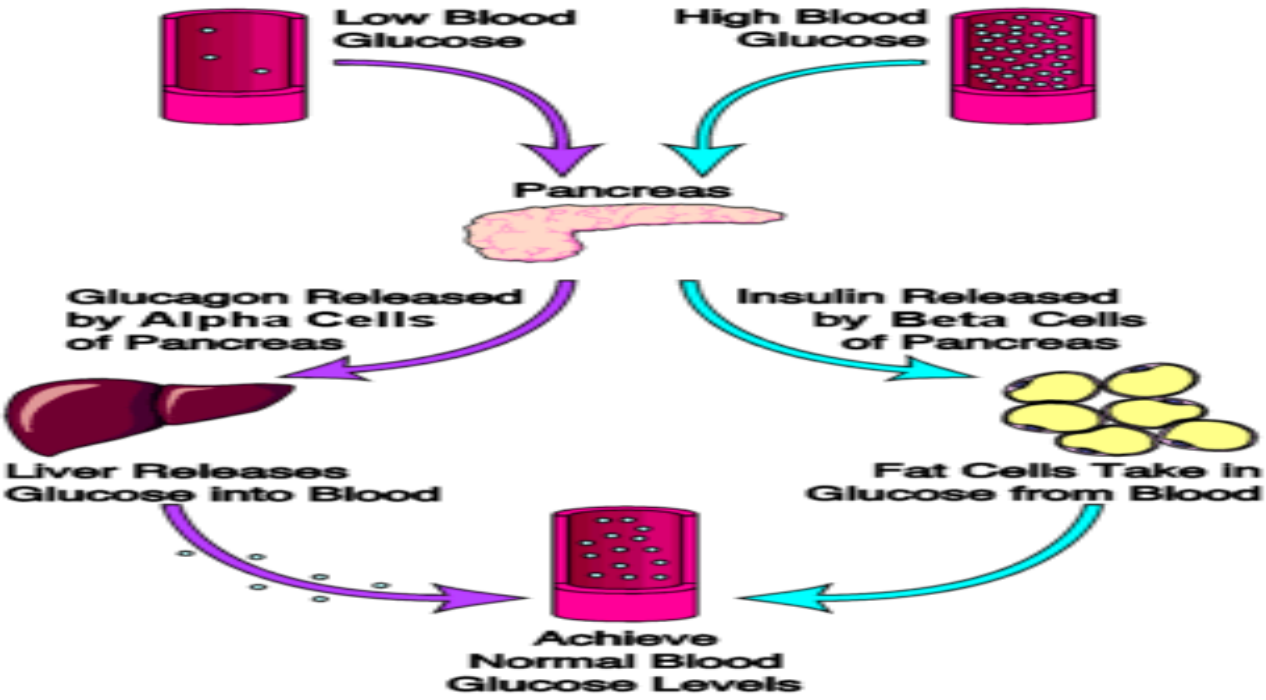

Figure1.1: role of glucagon and insulin to regulate blood sugar

(Endocrine web, *James Norman*)

1.5Types of diabetes

Diabetes mellitus (or diabetes) is a chronic, lifelong condition that affects body's ability to use the energy found in food. There are three major types of diabetes:

- Type 1 diabetes,
- Type 2 diabetes
- Gestational diabetes.

All types of diabetes mellitus have something in common. Normally, body breaks down the sugars and carbohydrates into a special sugar called glucose. Glucose fuels the cells in body. But the cells need insulin, a hormone, in your bloodstream in order to take in the glucose and use it for energy. With diabetes mellitus, either body doesn't make enough insulin; it can't use the insulin it does produce, or a combination of both.Since the cells can't take in the glucose, it builds up in blood. High levels of blood glucose can damage the tiny blood vessels in kidneys, heart, eyes, or nervous system. That's why diabetes especially if left untreated can eventually cause heart disease, stroke, kidney disease, blindness, and nerve damage to nerves in the feet (Dan singer MD 2014).

1.5.1 Type 1 Diabetes

Type 1 diabetes is also called insulin-dependent diabetes. It used to be called juvenile-onset diabetes, because it often begins in childhood. Type 1 diabetes is an autoimmune condition. It's caused by the body attacking its own pancreas with antibodies. In people with type 1 diabetes, the damaged pancreas doesn't make insulin. This type of diabetes may be caused by a genetic predisposition. It could also be the result of faulty beta cells in the pancreas that normally produce insulin. A number of medical risks are associated with type 1 diabetes. Many of them stem from damage to the tiny blood vessels in your eyes (called diabetic retinopathy), nerves (diabetic neuropathy), and kidneys (diabetic nephropathy). Even more serious is the increased risk of heart disease and stroke. A periodic test called the Hb A1C blood test estimates glucose levels in blood over the previous three months. It's used to help identify overall glucose level control and the risk of complications from diabetes, including organ damage.

Having type 1 diabetes does require significant lifestyle changes that include:

- Frequent testing of your blood sugar levels
- Careful meal planning
- Daily exercise
- Taking insulin and other medications as needed

People with type 1 diabetes can lead long, active lives if they carefully monitor their glucose, make the needed lifestyle changes, and adhere to the treatment plan. (Dan singer, MD2014)

HbA1C blood test

The A1C test is a blood test that provides information about a person’s average levels of blood glucose, also called blood sugar, over the past 3 months. The A1C test is sometimes called the hemoglobin A1C, HbA1c, or glycol hemoglobin test. The A1C test is the primary test used for diabetes management and diabetes research. The A1C test is based on the attachment of glucose to hemoglobin, the protein in red blood cells that carries oxygen. In the body, red blood cells are constantly forming and dying, but typically they live for about 3 months. Thus, the A1C test reflects the average of a person’s blood glucose levels over the past 3 months. The A1C test result is reported as a percentage. The higher the percentage, the higher a person’s blood glucose levels

have been. A normal A1C level is below 5.7 percent (National Institute of Diabetes and Digestive and Kidney Diseases 2014).

1.5.1.1 Patho physiology of type 1 diabetes mellitus

In autoimmune diseases, such as type 1 diabetes, the immune system mistakenly manufactures antibodies and inflammatory cells that are directed against and cause damage to patients' own body tissues. In persons with type 1 diabetes, the beta cells of the pancreas, which are responsible for insulin production, are attacked by the misdirected immune system. It is believed that the tendency to develop abnormal antibodies in type 1 diabetes is, in part, genetically inherited, though the details are not fully understood. Exposure to certain viral infections (mumps and Coxsackie viruses) or other environmental toxins may serve to trigger abnormal antibody responses that cause damage to the pancreas cells where insulin is made. Some of the antibodies seen in type 1 diabetes include anti-islet cell antibodies, anti-insulin antibodies and anti-glutamic decarboxylase antibodies. These antibodies can be detected in the majority of patients, and may help determine which individuals are at risk for developing type 1 diabetes.

At present, the American Diabetes Association does not recommend general screening of the population for type 1 diabetes, though screening of high risk individuals, such as those with a first degree relative (sibling or parent) with type 1 diabetes should be encouraged. Type 1 diabetes tends to occur in young, lean individuals, usually before 30 years of age, however, older patients do present with this form of diabetes on occasion. This subgroup is referred to as latent autoimmune diabetes in adults (LADA). LADA is a slow, progressive form of type 1 diabetes. Of all the people with diabetes, only approximately 10% have type 1 diabetes and the remaining 90% have type 2 diabetes (MedicineNet.com 2015).

1.5.1.2 Epidemiology and etiology

Type 1 and type 2 diabetes mellitus (T1D, T2D) have in common high blood glucose levels (hyperglycemia) that can cause serious health complications including ketoacidosis, kidney failure, heart disease, stroke, and blindness. Patients are often diagnosed with diabeteswhen they see a physician for clinical signs such as excessive thirst, urination, and hunger. These symptoms result from the underlying hyperglycemia that is in turn caused by insufficient insulin functionality. In Type2 Diabetes, which is usually associated with obesity or older age, this is mostly the result of

insulin resistance: the muscle or adipose cells do not respond adequately to normal levels of insulin produced by intact beta-cells. Type1Diabetes on the other hand usually starts in people younger than 30 and is therefore also termed juvenile-onset diabetes, even though it can occur at any age. Type1Diabetes is a chronic autoimmune disorder that precipitates in genetically susceptible individuals by environmental factors. The body's own immune system attacks the beta-cells in the islets of Langerhans of the pancreas, destroying or damaging them sufficiently to reduce and eventually eliminate insulin production. On rare but increasing occasions, both Type1Diabetes and Type2 Diabetes are diagnosed in patients. According to the American Center for Disease Control, 23.6 million People, 7.8% of the population, have Type1Diabetes or Type2 Diabetes, and 1.6 million new cases of diabetes were diagnosed in people aged 20 years or older in 2007. The Prevalence of Type1Diabetes for residents of the United States aged 0–19 years is 1.7/1,000. Type1Diabetes incidence has been globally rising during the past decades by as much as a 5.3% annually in the United States. If present trends continue, doubling of new cases of Type1Diabetes in European children younger than 5 years is predicted between 2005 and 2020, and prevalence of cases in individuals younger than 15years will rise by 70%, characteristic of a left shift towards an earlier age. This suggests that whatever event triggers the onset is increasingly affecting susceptible individuals. The search for such triggering factors has been ongoing for many years and has so far only yielded indirect evidence, predominantly implicating certain viral infections. It is now well established that a specific genetic constitution is required for such an event to cause diabetes. However, concordance rates between monozygotic twins amount to only 50%, whereas between dizygotic twins only 10%. With longer follow-up, the majority of discordant identical twins of patients with T1D eventually express anti-islet auto antibodies and progress to diabetes, but anti-islet auto antibodies in the second twin may appear only 30 years after the first twin develops diabetes. Thus it seems that genetic susceptibility persists for life, and progression to diabetes is usually preceded by a long prodrome of anti-islet autoantibody expression measured in years. Nevertheless, although the concordance rate for monozygotic twins is higher than previously thought, it is below unity, and there are strong divergences in terms of the time it takes to develop Type1Diabetes. This implies a strong environmental component to contribute to the development of Type1Diabetes. Since the early 1920s, diabetes has been treated by insulin replacement, which, in the ideal case, will only shorten life expectancy by 10 years. This sets a high safety bar for any immune-based intervention. Even more so, recent technology (continuous blood glucose monitors, slow release insulin, etc.) can reduce the chance for life-threatening hypoglycemic episodes from

insulin overdoses. Therefore, immune-based interventions should ideally be effective, long-lasting, and have minimal side effects to replace substitutive insulin treatment with a cure. Today, despite the many remaining challenges in the field of Type1Diabetes immunotherapy, good progress has been made (Tom L. Van Belle, et al 2011).

1.5.1.3 Causes of type 1 diabetes

Type 1 diabetes is caused by a lack of insulin due to the destruction of insulin-producing beta cells in the pancreas. In type 1 diabetes—an autoimmune disease—the body's immune system attacks and destroys the beta cells. Normally, the immune system protects the body from infection by identifying and destroying bacteria, viruses, and other potentially harmful foreign substances. But in autoimmune diseases, the immune system attacks the body's own cells. In type 1 diabetes, beta cell destruction may take place over several years, but symptoms of the disease usually develop over a short period of time. Type 1 diabetes typically occurs in children and young adults, though it can appear at any age. In the past, type 1 diabetes was called juvenile diabetes or insulin-dependent diabetes mellitus. Latent autoimmune diabetes in adults (LADA) may be a slowly developing kind of type 1 diabetes. Diagnosis usually occurs after age 30. In LADA, as in type 1 diabetes, the body's immune system destroys the beta cells. At the time of diagnosis, people with LADA may still produce their own insulin, but eventually most will need insulin shots or an insulin pump to control blood glucose levels.

Genetic Susceptibility

Heredity plays an important part in determining who is likely to develop type 1 diabetes. Genes are passed down from biological parent to child. Genes carry instructions for making proteins that are needed for the body's cells to function. Many genes, as well as interactions among genes, are thought to influence susceptibility to and protection from type 1 diabetes. The key genes may vary in different population groups. Variations in genes that affect more than 1 percent of a population group are called gene variants. Certain gene variants that carry instructions for making proteins called human leukocyte antigens (HLAs) on white blood cells are linked to the risk of developing type 1 diabetes. The proteins produced by HLA genes help determine whether the immune system recognizes a cell as part of the body or as foreign material. Some combinations of HLA gene variants predict that a person will be at higher risk for type 1 diabetes, while other combinations are protective or have no effect on risk. While HLA genes are the major risk genes for type 1 diabetes,

many additional risk genes or gene regions have been found. Not only can these genes help identify people at risk for type 1 diabetes, but they also provide important clues to help scientists better understand how the disease develops and identify potential targets for therapy and prevention. Genetic testing can show what types of HLA genes a person carries and can reveal other genes linked to diabetes. However, most genetic testing is done in a research setting and is not yet available to individuals. Scientists are studying how the results of genetic testing can be used to improve type 1 diabetes prevention or treatment (National Diabetes Statistics Report, 2014).

Autoimmune Destruction of Beta Cells

In type 1 diabetes, white blood cells called T cells attack and destroy beta cells. The process begins well before diabetes symptoms appear and continues after diagnosis. Often, type 1 diabetes is not diagnosed until most beta cells have already been destroyed. At this point, a person needs daily insulin treatment to survive. Finding ways to modify or stop this autoimmune process and preserve beta cell function is a major focus of current scientific research. Recent research suggests insulin itself may be a key trigger of the immune attack on beta cells. The immune systems of people who are susceptible to developing type 1 diabetes respond to insulin as if it were a foreign substance, or antigen. To combat antigens, the body makes proteins called antibodies. Antibodies to insulin and other proteins produced by beta cells are found in people with type 1 diabetes. Researchers test for these antibodies to help identify people at increased risk of developing the disease. Testing the types and levels of antibodies in the blood can help determine whether a person has type 1 diabetes, LADA, or another type of diabetes.

Environmental Factors

Environmental factors, such as foods, viruses, and toxins, may play a role in the development of type 1 diabetes, but the exact nature of their role has not been determined. Some theories suggest that environmental factors trigger the autoimmune destruction of beta cells in people with a genetic susceptibility to diabetes. Other theories suggest that environmental factors play an ongoing role in diabetes, even after diagnosis.

Viruses and infections

A virus cannot cause diabetes on its own, but people are sometimes diagnosed with type 1 diabetes during or after a viral infection, suggesting a link between the two. Also, the onset of type 1 diabetes occurs more frequently during the winter when viral infections are more common. Viruses possibly associated with type 1 diabetes include coxsackievirus B, cytomegalovirus, adenovirus, rubella, and mumps. Scientists have described several ways these viruses may damage or destroy beta cells or possibly trigger an autoimmune response in susceptible people. For example, anti-islet antibodies have been found in patients with congenital rubella syndrome, and cytomegalovirus has been associated with significant beta cell damage and acute pancreatitis inflammation of the pancreas. Scientists are trying to identify a virus that can cause type 1 diabetes so that a vaccine might be developed to prevent the disease.4 Causes of Diabetes

Infant feeding practices

Some studies have suggested that dietary factors may raise or lower the risk of developing type 1 diabetes. For example, breastfed infants and infants receiving vitamin D supplements may have a reduced risk of developing type 1 diabetes, while early exposure to cow's milk and cereal proteins may increase risk. More research is needed to clarify how infant nutrition affects the risk for type 1 diabetes. (Centre's for National Diabetes Statistics Report, 2014)

1.5.1.4 Signs and symptoms

Type 1 diabetes signs and symptoms can come on quickly and may include:

- Increased thirst
- Frequent urination
- Bedwetting in children who previously didn't wet the bed during the night
- Extreme hunger
- Unintended weight loss
- Irritability and other mood changes
- Fatigue and weakness
- Blurred vision
- In females, a vaginal yeast infection (Mayo clinic 2014).

1.5.1.5 Diagnosis

Table1.1: Diagnostic criteria by the American Diabetes Association (ADA):

A fasting plasma glucose (FPG) level	≥126 mg/dL (7.0 mmol/L)
A 2-hour plasma glucose level	≥200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT)
A random plasma glucose	≥200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis

A finger stick glucose test is appropriate for virtually all patients with diabetes. All finger stick capillary glucose levels must be confirmed in serum or plasma to make the diagnosis. All other laboratory studies should be selected or omitted on the basis of the individual clinical situation.

An international expert committee appointed by the ADA, the European Association for the Study of Diabetes, and the International Diabetes Association recommended the Hb A1c assay for diagnosing type 1 diabetes only when the condition is suspected but the classic symptoms are absent

1.5.1.6 Management

Glycemic control

The ADA recommends using patient age as one consideration in the establishment of glycemic goals, with different targets for pre-prandial, bedtime/overnight, and hemoglobin A1C (HbA1c) levels in patients aged 0-6, 6-12, and 13-19 years. Benefits of tight glycemic control include not only continued reductions in the rates of micro vascular complications but also significant differences in cardiovascular events and overall mortality.

Self-monitoring

Optimal diabetic control requires frequent self-monitoring of blood glucose levels, which allows rational adjustments in insulin doses. All patients with type 1 diabetes should learn how to self-monitor and record their blood glucose levels with home analyzers and adjust their insulin doses accordingly.Real-time continuous monitoring of glucose using continuous glucose monitors (CGMs) can help patients improve glycemic control. CGMs contain subcutaneous sensors that measure interstitial glucose levels every 1-5 minutes, providing alarms when glucose levels are too high or too low or are rapidly rising or falling.

Insulin therapy

Patients with type 1 diabetes require lifelong insulin therapy. Most require 2 or more injections of insulin daily, with doses adjusted on the basis of self-monitoring of blood glucose levels. Insulin replacement is accomplished by giving basal insulin and a pre-prandial (premeal) insulin. The basal insulin is either long-acting (glargine or detemir) or intermediate-acting (NPH). The pre-prandial insulin is either rapid-acting (lispro, aspart, insulin inhaled, or glulisine) or short-acting (regular).

Common insulin regimens include the following:

Split or mixed: NPH with rapid-acting (e.g., lispro, aspart, or glulisine) or regular insulin before breakfast and supper

Split or mixed variant: NPH with rapid-acting or regular insulin before breakfast, rapid-acting or regular insulin before supper, and NPH before bedtime (the idea is to reduce fasting hypoglycemia by giving the NPH later in the evening)

Multiple daily injections (MDI): A long-acting insulin (e.g., glargine or detemir) once a day in the morning or evening (or twice a day in about 20% of patients) and a rapid-acting insulin before meals or snacks (with the dose adjusted according to the carbohydrate intake and the blood glucose level)

Continuous subcutaneous insulin infusion (CSII): Rapid-acting insulin infused continuously 24 hours a day through an insulin pump at 1 or more basal rates, with additional boluses given before each meal and correction doses administered if blood glucose levels exceed target levels

Diet and activity

All patients on insulin should have a comprehensive diet plan, created with the help of a professional dietitian that includes the following:

A daily caloric intake prescription Recommendations for amounts of dietary carbohydrate, fat, and protein Instructions on how to divide calories between meals and snacks. Exercise is also an important aspect of diabetes management. Patients should be encouraged to exercise regularly (Romesh Khardori, 2015).

1.5.2 Type 2 Diabetes

By far, the most common form of diabetes is type 2 diabetes, accounting for 95% of diabetes cases in adults. Some 26 million American adults have been diagnosed with the disease. Type 2 diabetes used to be called adult-onset diabetes, but with the epidemic of obese and overweight kids, more teenagers are now developing type 2 diabetes. Type 2 diabetes was also called non-insulin-dependent diabetes. Type 2 diabetes is often a milder form of diabetes than type 1. Nevertheless, type 2 diabetes can still cause major health complications, particularly in the smallest blood vessels in the body that nourish the kidneys, nerves, and eyes. Type 2 diabetes also increases your risk of heart disease and stroke. With Type 2 diabetes, the pancreas usually produces some insulin. But either the amount produced is not enough for the body's needs, or the body's cells are resistant to it. Insulin resistance, or lack of sensitivity to insulin, happens primarily in fat, liver, and muscle cells. People who are obese more than 20% over their ideal body weight for their height -- are at particularly high risk of developing type 2 diabetes and its related medical problems. Obese people are insulin resistance. With insulin resistance, the pancreas has to work overly hard to produce more insulin. But even then, there is not enough insulin to keep sugars normal. Type 2 diabetes can, however, be controlled with weight management, nutrition, and exercise. Unfortunately, type 2 diabetes tends to progress, and diabetes medications are often needed. An HbA1C test is a blood test that estimates average glucose levels in blood over the previous three months. Periodic HbA1C testing may be advised to see how well diet, exercise, and medications are working to control blood sugar and prevent organ damage. The HbA1C test is typically done a few times a year. (Michael Dan singer, MD 2014)

1.5.2.1 Patho physiology of type 2 diabetes

Type 2 diabetes was also previously referred to as non-insulin dependent diabetes mellitus (NIDDM), or adult onset diabetes mellitus (AODM). In type 2 diabetes, patients can still produce insulin, but do so relatively inadequately for their body's needs, particularly in the face of insulin resistance as discussed above. In many cases this actually means the pancreas produces larger than normal quantities of insulin. A major feature of type 2 diabetes is a lack of sensitivity to insulin by the cells of the body (particularly fat and muscle cells). In addition to the problems with an increase in insulin resistance, the release of insulin by the pancreas may also be defective and suboptimal. In fact, there is a known steady decline in beta cell production of insulin in type 2 diabetes that contributes to worsening glucose control. (This is a major factor for many patients with type 2 diabetes who ultimately require insulin therapy.) Finally, the liver in these patients continues to produce glucose through a process called gluconeogenesis despite elevated glucose levels. The control of gluconeogenesis becomes compromised. While it is said that type 2 diabetes occurs mostly in individuals over 30 years old and the incidence increases with age, we are seeing an alarming number patients with type 2 diabetes who are barely in their teen years. Most of these cases are a direct result of poor eating habits, higher body weight, and lack of exercise. While there is a strong genetic component to developing this form of diabetes, there are other risk factors - the most significant of which is obesity. There is a direct relationship between the degree of obesity and the risk of developing type 2 diabetes, and this holds true in children as well as adults. It is estimated that the chance to develop diabetes doubles for every 20% increase over desirable body weight (MedicineNet.com 2015).

1.5.2.2 Epidemiology of type 2 diabetes

In the last two decades, type 2 diabetes, once thought to be a metabolic disorder exclusively of adulthood, has become increasingly more frequent in obese adolescents (J Pediatr 2005).Although a very high prevalence of type 2 diabetes has been observed in non-Caucasian groups (African Americans, Native Americans, Hispanics), type 2 diabetes occurs in all races (Rosenbloom AL 2009). In the SEARCH study (D'Agostino RB Jr, et al 2007), the incidence rate (per 100,000 person-year) of type 2 diabetes among children and adolescents varies greatly by ethnicity, with the highest rates observed among youths aged 15–19 years in minority populations. In particular, the reported incidence rate was 49.4 for Native Americans, 22.7 for Asian/Pacific Islanders, 19.4 for

African Americans, 17 for Hispanics, and 5.6 for non-Hispanic whites. Type 2 diabetes in youth is not just an American phenomenon more cases are being reported worldwide. For example, in Japan (J Pediatr 2005) 80% of all new cases of diabetes in children and adolescents were diagnosed as type 2 diabetes. Likewise,in Taiwan (J Pediatr 2005) 54.2% of new cases were diagnosed with type 2 diabetes, with an incidence of 6.5 per 100,000. In contrast, in the U.K. the minimum incidence of type 2 diabetes in children (, 17 years of age) was 0.53 z 100,00021 z year21 (Haines L 2007).In Austria, the calculated incidence of type 2 diabetes in children and adolescents (,15 years of age) was 0.25/100,000 (J Pediatr 2005). Indeed, many studies from Europe (D'Agostino RB Jr, et al 2007) indicate that type 2 diabetes is not as common as in the U.S. in these populations, accounting for only 1–2% of all diabetes mellitus cases. In addition, although some studies(D'Agostino RB Jr, et al 2007) support the notion that type 2 diabetes has a greater prevalence in the high risk ethnic groups, type 2 diabetes accounts for 14.9% of all diabetes cases among non-Hispanic white adolescents . Although the lowest prevalence of type 2 diabetes, observed in Europe, could be attributed to the differences in obesity rates between U.S. and European youth, the full explanation for these discrepancies remains unclear (D'Agostino RB Jr, et al 2007).The increased prevalence of type 2 diabetes in the obese pediatric population is paralleled by an increased prevalence of the prediabetes conditions. In particular, 25% of children and 21% adolescents with severe degree of obesity, irrespective of ethnicity, were found to have IGT .Similar high prevalence rates in Hispanic obese children and adolescents were subsequently reported by Goran et al. (Goran MI et al).Surprisingly, very high prevalence rates of IFG were reported in children from the Studies to Treat or Prevent Pediatric Type 2 Diabetes (2).Although previous studies showed a lower prevalence of type 2 diabetes and IGT in Italian youths (0.5% and 5%, respectively) (Invitti C et al 2002), a recent study conducted in Italy on a large sample of overweight/obese children and adolescents reported a prevalence of glucose metabolism alterations of 12.4%. IGT was the most frequent alteration, accounting for 11.2%, with a higher prevalence in adolescents (14.8%) than in children (4.1%) (Brufani C, et al 2010).

1.5.2.3 Causes of type 2 diabetes

Type 2 diabetes the most common form of diabetes is caused by a combination of factors, including insulin resistance, a condition in which the body's muscle, fat, and liver cells do not use insulin effectively. Type 2 diabetes develops when the body can no longer produce enough insulin to

compensate for the impaired ability to use insulin. Symptoms of type 2 diabetes may develop gradually and can be subtle; some people with type 2 diabetes remain undiagnosed for years. Type 2 diabetes develops most often in middle-aged and older people who are also overweight or obese. The disease, once rare in youth, is becoming more common in overweight and obese children and adolescents. Scientists think genetic susceptibility and environmental factors are the most likely triggers of type 2 diabetes.

Genetic Susceptibility

Genes play a significant part in susceptibility to type 2 diabetes. Having certain genes or combinations of genes may increase or decrease a person's risk for developing the disease. The role of genes is suggested by the high rate of type 2 diabetes in families and identical twins and wide variations in diabetes prevalence by ethnicity. Type 2 diabetes occurs more frequently in African Americans, Alaska Natives, American Indians, Hispanics/Latinos, and some Asian Americans, Native Hawaiians, and Pacific Islander Americans than it does in non- Hispanic whites.

Recent studies have combined genetic data from large numbers of people, accelerating the pace of gene discovery. Though scientists have now identified many gene variants that increase susceptibility to type 2 diabetes, the majority have yet to be discovered. The known genes appear to affect insulin production rather than insulin resistance. Researchers are working to identify additional gene variants and to learn how they interact with one another and with environmental factors to cause diabetes. Studies have shown that variants of the

TCF7L2 gene increase susceptibility to type 2 diabetes. For people who inherit two copies of the variants, the risk of developing type 2 diabetes is about 80 percent higher than for those who do not carry the gene variant.1 However, even in those with the variant, diet and physical activity leading to weight loss help delay diabetes, according to the Diabetes Prevention Program (DPP), a major clinical trial involving people at high risk. (Grant RW, et al 2009)

Obesity and Physical Inactivity

Physical inactivity and obesity are strongly associated with the development of type 2 diabetes. People who are genetically susceptible to type 2 diabetes are more vulnerable when these risk factors are present. An imbalance between caloric intake and physical activity can lead to obesity, which causes insulin resistance and is common in people with type 2 diabetes. Central obesity, in

which a person has excess abdominal fat, is a major risk factor not only for insulin resistance and type 2 diabetes but also for heart and blood vessel disease, also called cardiovascular disease (CVD). This excess "belly fat" produces hormones and other substances that can cause harmful, chronic effects in the body such as damage to blood vessels. The DPP and other studies show that millions of people can lower their risk for type 2 diabetes by making lifestyle changes and losing weight. The DPP proved that people with pre diabetes at high risk of developing type 2 diabetes could sharply lower their risk by losing weight through regular physical activity and a diet low in fat and calories. In 2009, a follow-up study of DPP participants the Diabetes Prevention Program Outcomes Study (DPPOS) showed that the benefits of weight loss lasted for at least 10 years after the original study began (Lancet. 2009).

Insulin Resistance

Insulin resistance is a common condition in people who are overweight or obese, have excess abdominal fat, and are not physically active. Muscle, fat, and liver cells stop responding properly to insulin, forcing the pancreas to compensate by producing extra insulin. As long as beta cells are able to produce enough insulin, blood glucose levels stay in the normal range. But when
Insulin production falters because of beta cell dysfunction, glucose levels rise, leading to
Pre diabetes or diabetes (National Institute Of Diabetes and digestive kidney disease 2009)

Abnormal Glucose Production by the Liver:

In some people with diabetes, an abnormal increase in glucose production by the liver also contributes to high blood glucose levels. Normally, the pancreas releases the hormone glucagon when blood glucose and insulin levels are low. Glucagon stimulates the liver to produce glucose and release it into the bloodstream. But when blood glucose and insulin levels are high after a meal, glucagon levels drop, and the liver stores excess glucose for later, when it is needed. For reasons not completely understood, in many people with diabetes, glucagon levels stay higher than needed. High glucagon levels cause the liver to produce unneeded glucose, which contributes to high blood glucose levels. Metformin, the most commonly used drug to treat type 2 diabetes, reduces glucose production by the liver (National Institute of Diabetes and digestive kidney disease 2009).

1.5.2.4 Signs and symptoms:

Type 2 diabetes symptoms often develop slowly. They are given bellow:

Increased thirst and frequent urination:

Excess sugar building up in bloodstream causes fluid to be pulled from the tissues. This may leave thirsty. As a result, one may drink and urinate more than usual.

Increased hunger:

Without enough insulin to move sugar into cells, muscles and organs become depleted of energy. This triggers intense hunger.

Weight loss:

Despite eating more than usual to relieve hunger, one may lose weight. Without the ability to metabolize glucose, the body uses alternative fuels stored in muscle and fat. Calories are lost as excess glucose is released in the urine.

Fatigue:

If cells are deprived of sugar, one may become tired and irritable.

Blurred vision:

If blood sugar is too high, fluid may be pulled from the lenses of your eyes. This may affect ability to focus.

Slow-healing sores or frequent infections:

Type 2 diabetes affects ability to heal and resist infections.

Areas of darkened skin:

Some people with type 2 diabetes have patches of dark, velvety skin in the folds and creases of one's bodies usually in the armpits and neck. This condition, called acanthosis nigricans, may be a sign of insulin resistance (Mayo clinic2014).

1.5.2.5 Diabetes management

Food

- **Make every meal well-balanced.** As much as possible, plan for every meal have to be a good mix of starches, fruits and vegetables, proteins, and fats. It's especially important to pay attention to the types of carbohydrates you choose. Some carbohydrates, such as fruits, vegetables and whole grains, are better for health than others. These foods are low in carbohydrates and contain fiber that helps keep blood sugar levels more stable.
- **Coordination of meals and medications.** Too little food in proportion to diabetes medications especially insulin may result in dangerously low blood sugar (hypoglycemia). Too much food may cause blood sugar level to climb too high (hyperglycemia). So one should talk to diabetes health care team about how to best coordinate meal and medication schedules.
- **Avoid sugar-sweetened beverages.** Sugar-sweetened beverages including those sweetened with high fructose corn syrup or sucrose tend to be high in calories and offer little in the way of nutrition. And because they cause blood sugar to rise quickly, it's best to avoid these types of drinks if one has diabetes.

  The exception is if one is experiencing a low blood sugar level. Sugar-sweetened beverages, such as soda, juice and sports drinks can be used as an effective treatment for quickly raising blood sugar that is too low.

Exercise:

Physical activity is another important part of your diabetes management plan. At the time of exercise, muscles use sugar (glucose) for energy. Regular physical activity also helps body to use insulin more efficiently.

These factors work together to lower blood sugar level. The more strenuous workout, the longer the effect lasts. But even light activities such as housework, gardening or being on your feet for extended periods can improve blood sugar level.

What to do:

- **Exercise plan.** Doctor should be asked about what type of exercise is appropriate for patient. In general, most adults should exercise at least 30 minutes a day on most days of the week. If one

has been inactive for a long time, doctor may want to check your overall health before advising you. He or she can recommend the right balance of aerobic and muscle-strengthening exercise.

- **Exercise schedule can be kept:** One should talk to doctor about the best time of day for exercise so that workout routine is coordinated with meal and medication schedules.
- **Blood sugar level checking:** Blood sugar level should be checked before, during and after exercise, especially if insulin or medications are taken that lower blood sugar level. Exercise can lower your blood sugar levels even a day later, especially if the activity is new, or if one is exercising at a more intensive level. Should be conscious about warning signs of low blood sugar, such as feeling shaky, weak, tired, hungry, lightheaded, irritable, anxious or confused.

  If one use insulin and blood sugar level is below 100 milligrams per deciliter (mg/dL), or 5.6 mill moles per liter (mmol/L), have a small snack before start exercising to prevent a low blood sugar level.

- **Hydration:** Plenty of water or other fluids should drink during exercising because dehydration can affect blood sugar levels.
- **Consciousness:** One should have always a small snack or glucose tablet during exercise in case of dropping blood sugar level.
- **Diabetes treatment plan should be adjusted:** If one takes insulin may need to reduce insulin dose before exercising or wait a while after exercise to inject insulin. Doctor can advise on appropriate changes in medication. One may also need to adjust treatment if one has increased exercise routine.

Medication

Insulin and other diabetes medications are designed to lower blood sugar levels when diet and exercise alone aren't sufficient for managing diabetes. But the effectiveness of these medications depends on the timing and size of the dose. Medications taken for conditions other than diabetes also can affect blood sugar levels.

What to do:

- **Proper Insulin storage:** Insulin that's improperly stored or past its expiration date may not be effective. Insulin is especially sensitive to extremes in temperature.

- **Problems should be reported to doctor:** If diabetes medications cause blood sugar level to drop too low or if it's consistently too high, the dosage or timing may need to be adjusted.
- **Should be cautious with new medications.** If considered an over-the-counter medication or doctor prescribes a new drug to treat another condition such as high blood pressure or high cholesterol doctor or pharmacist should be asked if the medication may affect blood sugar levels. Liquid medications may be sweetened with sugar to cover their taste. Sometimes an alternate medication may be recommended. Doctor should always be asked before taking any new over-the-counter medication, so one knows how it may impact blood sugar.(Mayo clinic 2014)

1.5.3 Gestational Diabetes

Diabetes that's triggered by pregnancy is called gestational diabetes (pregnancy, to some degree, leads to insulin resistance). It is often diagnosed in middle or late pregnancy. Because high blood

sugar levels in a mother are circulated through the placenta to the baby, gestational diabetes must be controlled to protect the baby's growth and development. According to the National Institutes of Health, the reported rate of gestational diabetes is between 2% to 10% of pregnancies. Gestational diabetes usually resolves itself after pregnancy. Having gestational diabetes does, however, put mothers at risk for developing type 2 diabetes later in life. Up to 10% of women with gestational diabetes develop type 2 diabetes. It can occur anywhere from a few weeks after delivery to months or years later.

With gestational diabetes, risks to the unborn baby are even greater than risks to the mother. Risks to the baby include abnormal weight gain before birth, breathing problems at birth, and higher obesity and diabetes risk later in life. Risks to the mother include needing a cesarean section due to an overly large baby, as well as damage to heart, kidney, nerves, and eye.

Treatment during pregnancy includes working closely with health care team:

- Careful meal planning to ensure adequate pregnancy nutrients without excess fat and calories
- Daily exercise
- Controlling pregnancy weight gain

- Taking diabetes insulin to control blood sugar levels if needed (Michael Dan singer, MD 2014)

1.5.3.1 Causes of gestational diabetes

Scientists believe gestational diabetes is caused by the hormonal changes and metabolic demands of pregnancy together with genetic and environmental factors.

Insulin Resistance and Beta Cell Dysfunction

Hormones produced by the placenta and other pregnancy-related factors contribute to insulin resistance, which occurs in all women during late pregnancy. Insulin resistance increases the amount of insulin needed to control blood glucose levels. If the pancreas can't produce enough insulin due to beta cell dysfunction, gestational diabetes occurs. As with type 2 diabetes, excess weight is linked to gestational diabetes. Overweight or obese women are at particularly high risk for gestational diabetes because they start pregnancy with a higher need for insulin due to insulin resistance. Excessive weight gain during pregnancy may also increase risk. (National diabetes statistics report, 2014)

Family History

Having a family history of diabetes is also a risk factor for gestational diabetes, suggesting that genes play a role in its development. Genetics may also explain why the disorder occurs more frequently in African Americans, American Indians, and Hispanics/Latinos. Many gene variants or combinations of variants may increase a woman's risk for developing gestational diabetes. Studies have found several gene variants associated with gestational diabetes, but these variants account for only a small fraction of women with gestational diabetes. (National diabetes statistics report, 2014)

1.5.3.2 Management of gestational diabetes:

Good glycogenic control has special importance during pregnancy. Maternal and perinatal complications can be reduced if good control is achieved before and during conception. Good biochemical control before pregnancy is important since hyperglycemia seems to be a major factor in the development of congenital malformations and the risk of these malformations is highest during the first eight weeks of gestation. Intensive education and management of the woman with diabetes should start several months before conception to ensure strict control during the early

weeks of pregnancy. Pregnancy may have to be deferred until optimal control is achieved. Women well controlled on oral hypoglycemic drugs should be changed over to insulin and achieve optimal blood glucose control before conception. Those well controlled on diet alone may continue on such therapy as long as they are carefully monitored to assess the need for insulin. Therapy targets, prior to conception, should be achieved. Treatment should aim at having pre-prandial and postprandial glucose levels which are close to normal as well as normal or near normal glycated hemoglobin levels (if such measurement is available). Full clinical assessment is needed. Renal and retinal complications should be looked for.Ophthalmoscopy and testing for urinary albumin should be repeated during pregnancy. During pregnancy, frequent follow-up is needed to ensure that therapy targets are met without significant hypoglycemia. Review every two to four weeks is generally recommended but should be more frequent if required.

1.5.3.3 Screening for diabetes during pregnancy

A substantial proportion of women of childbearing age develop gestational diabetes mellitus (GDM). GDM is defined as diabetes which is first detected during pregnancy. In order to prevent maternal and perinatal complications of diabetes, early detection of glucose tolerance abnormalities during pregnancy is important. Another advantage in screening for GDM is the fact that women who develop glucose intolerance during pregnancy will run a higher risk of developing diabetes in the future; thus, detection of this abnormality provides the possibility of preventive intervention. The following recommendations on screening for GDM during pregnancy in the Eastern Mediterranean Region were made during the First WHO Regional Meeting on Diabetes in 1992:

Screening is recommended at two stages during pregnancy:

• All pregnant women should be screened for diabetes during the first antenatal visit by

testing for glycosuria. A positive test is an indication for further assessment by a 75 g

Oral glucose tolerance test.

• At 24-28 weeks of gestation, women at high risk of developing GDM or IGT should be

screened by means of an oral glucose tolerance test, using 75 g glucose load.

Those at high risk include women with:

— Previous GDM or IGT

— A family history of diabetes

— Obesity (World Health organization 1994).

1.5.4 Diabetes insipidus:

Diabetes insipidus (DI) causes frequent urination becoming extremely thirsty, so after drinking one can urinate. This cycle can keep one from sleeping or even make wet the bed and body produces lots of urine that is almost all water. Diabetes insipidus is different from diabetes mellitus (DM), which involves insulin problems and high blood sugar. The symptoms can be similar. However, DI is related to how your kidneys handle fluids. It's much less common than DM. Urine and blood tests can show the specific type. Usually, DI is caused by a problem with your pituitary gland or your kidneys. Treatment depends on the cause of the problem. Medicines can often help.(Department of Health and Human Services National Institutes of Health 2014)

1.6 Anti-diabetic drugs:

Classification of oral ant diabetic medication:

- Sulfonylurea's:
    - Generation I: Tolbutamide, Chlorpropamide, Tolazamide.
    - Generation II: Glibenclamide, Glipizide, Gliclazide, Gliquidone.
    - Generation III: Glimepiride.
- Biguanides: Metformin, Buformin.
- Thiazolidinediones: Pioglitazone, Rosiglitazone.
- Meglitinides: Repaglinide, Nateglinide.
- Alpha glucosidase inhibitors: Acarbose, Miglitol, Voglibose.
- New antidiabetic drugs: Exenatide (Byetta), Sitagliptin (Januvia).

2.1 Cutaneous manifestation of diabetes mellitus

One hundred consecutive diabetes mellitus patients attending the diabetic clinic of the hospital constituted the study group. One hundred age and sex matched non-diabetics were taken as controls. The majority, 63%, belonged to the 41-60 years age group and 98% had non-insulin dependent diabetes. Among the study group, 64% had one or more cutaneous manifestations as compared to 22% in the controls. This was statistically highly significant ($p<0,001$). Infections comprised the largest group affecting 35 of the 64 cases. Among the bacterial infections, pyodermas were observed in 11 and erythrasma in one. Fungal infections were seen in 21, dermatophytoses in 11, and candidiasis in 10. Herpes zoster was seen in 2 cases. Pruritus was observed in 10, neurological abnormalities in the form of paresthesias was seen in 6, mal perforans in one, and meralgiaparesthetica in one. Diabetic dermopathy was seen in 6 and rubeosis in 4. Six dermatoses strongly associated with DM were seen, namely one each of waxy skin syndrome, granuloma annulare, eruptive xanthoma, scleredemaadultorum, and 2 cases of diabetic bulla.Ten patients exhibited other dermotoses less associated with diabetics: xanthelasmopalpebrarum in 5 patients, acrochordi in 4, and pigmented purpuricdermatoses in one. Likewise syndromes of insulin resistance were seen in 4 patients of whom 3 had aconthosisnigricans and one had congenital lipodystrophy. Forthermore,9 patients had dermatoses known to be associated with an increased incidence of diabetes; vitiligo in 4, acquired perforating dermatoses in 3, and lichen planus in 2. Four patients hoddermatoses known to be associated with diabetes: psoriasis in 3 and diffuse alopecia in one. Three had adverse drug reactions to anti-diabetic therapy (mahaajan &Sharma 2003).

2.2 Collation and comparison of multi-practice audit data: prevalence and treatment of known diabetes mellitus.

Different methods have been used to determine the prevalence and treatment of diabetes. Despite the large number of studies, previous estimations of prevalence and treatment have been carried out on relatively small numbers of patients, and then in only a few practices in single geographical regions. Investigating the feasibility of collating data from multi-practice audits organized by primary care audit groups in order to estimate the prevalence and treatment of patients with known diabetes, and to discuss the methodological issues and reasons for variation. A postal questionnaire survey of all primary care audit groups in England and Wales that had conducted a multi-practice audit of diabetes between 1993-1995. Prevalence rates and patterns of diabetic care

were compared with other community-based surveys of known diabetes from 1986-1996 identified on MEDLINE. RESULTS: Twenty-five (43%) audit groups supplied data from multi-practice audits of diabetes. Seven (28%) multi-practice audits involving 259 practices fulfilled the inclusion criteria for prevalence estimation. The overall prevalence of diabetes based on a population of 1,475,512 patients was 1.46% (range between audit groups = 1.18% to 1.66%; chi 2 = 308; df = 6; P < 0.0001). Male to female ratio was 1.15:1. Treatment of diabetes could be ascertained for 10 (40%) audit groups comprising 319 practices. Of these, 23.4% (range = 16.5%-27.4%) were controlled by diet, 48.5% (range = 43.6%-55.8%) were prescribed oral hypoglycaemic drugs, and 28.2% (range = 25.0%-32.4%) were treated with insulin. There were significant variations between audit groups in treatment pattern (chi 2 = 250; df = 18; P < 0.0001). Prevalence and treatment rates of diabetes and other chronic diseases can be assessed and compared using data from multi-practice audits. Collation of audit data could improve the precision of quantitative estimates of health status in populations. A standard method of data recording and collection may provide a new approach that could considerably improve our ability to monitor disease and its management (Khunti, goyder et al. 1999).

2.3 Lipid Control in the Management of Type 2 Diabetes Mellitus: A Clinical Practice Guideline from the American College of Physicians

In an effort to provide internists and other primary care physicians with effective management strategies for diabetes care, the Clinical Efficacy Assessment Subcommittee (CEAS) of the American College of Physicians (ACP) decided to develop guidelines on the management of dyslipidemia, particularly hypercholesterolemia, in people with type 2 diabetes mellitus. The CEAS commissioned a systematic review of the currently available evidence on the management of lipids in type 2 diabetes mellitus. The evidence review is presented in a background paper in this issue. On the basis of this systematic review, the CEAS developed recommendations that the ACP Board of Regents then approved as policy.The target audience for this guideline is all clinicians who care for patients with type 2 diabetes. The target patient population is all persons with type 2 diabetes, including those who already have some form of microvascular complication and, of particular importance, premenopausal women. The recommendations are as follows.*Recommendation 1: Lipid-lowering therapy should be used for secondary prevention of cardiovascular mortality and morbidity for all patients (both men and women) with known coronary artery disease and type 2 diabetes.Recommendation 2: Statins should be used for primary prevention against macrovascular*

complications in patients (both men and women) with type 2 diabetes and other cardiovascular risk factors.Recommendation given the markedly elevated risk for cardiovascular events in most persons with type 2 diabetes, preventing cardiovascular disease through aggressive management of cardiovascular risk factors is of utmost importance. Optimizing treatment of hypertension, smoking cessation, and lipid control provides substantial benefit, at least to the average patient with type 2 diabetes. The evidence suggests that lipid-lowering medication leads to a 22% to 24% reduction in major cardiovascular events in patients with diabetes. On the basis of the current literature, statins are the agents of choice. The meta-analysis by Vijan and colleagues suggests that there is good evidence for the empirical use of at least moderate doses of statins in patients at average or above-average risk for cardiovascular disease (Vincenza,Aroson et. al. 2004).

2.4 Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study

To examine whether intensive glycemic control could decrease the frequency or severity of diabetic microvascular complications, we performed a prospective study of Japanese patients with non-insulin-dependent diabetes mellitus (NIDDM) treated with multiple insulin injection treatment. A total of 110 patients with NIDDM was randomly assigned to multiple insulin injection treatment group (MIT group) or to conventional insulin injection treatment group (CIT group). Fifty-five NIDDM patients who showed no retinopathy and urinary albumin excretions <30 mg/24 h at the baseline were evaluated in the primary-prevention cohort, and the other 55 NIDDM patients who showed simple retinopathy and urinary albumin excretions <300 mg/24 h were evaluated in the secondary-intervention cohort. The appearance and the progression of retinopathy, nephropathy and neuropathy were evaluated every 6 months over a 6-year period. The worsening of complications in this study was defined as an increase of 2 or more steps in the 19 stages of the modified ETDRS interim scale for retinopathy and an increase of one or more steps in 3 stages (normoalbuminuria, microalbuminuria and albuminuria) for nephropathy. The cumulative percentages of the development and the progression in retinopathy after 6 years were 7.7% for the MIT group and 32.0% for the CIT group in the primary-prevention cohort (P = 0.039), and 19.2% for MIT group and 44.0% for CIT group in the secondary-intervention cohort (P = 0.049). The cumulative percentages of the development and the progression in nephropathy after 6 years were 7.7% for the MIT group and 28.0% for the CIT group in the primary-prevention cohort (P = 0.032), and 11.5%

and 32.0%, respectively, for the MIT and CIT groups in the secondary-intervention cohort (P = 0.044). In neurological tests after 6 years, MIT group showed significant improvement in the nerve conduction velocities, while the CIT group showed significant deterioration in the median nerve conduction velocities and vibration threshold. Although both postural hypotension and the coefficient of variation of R-R interval tended to improve in the MIT group, they deteriorated in the CIT group. In conclusion, intensive glycemic control by multiple insulin injection therapy can delay the onset and the progression of diabetic retinopathy, nephropathy and neuropathy in Japanese patients with NIDDM. From this study, the glycemic threshold to prevent the onset and the progression of diabetic microangiopathy is indicated as follows; HbA_1c < 6.5%, FBG < 110 mg/dl, and 2-h post-prandial blood glucose concentration <180 mg/dl (Ohkubo &Isami 1995).

2.5 Patient and physician perspectives regarding treatment of diabetes: compliance with practice guidelines.

Managed care organizations are focusing on how physicians manage their patients with diabetes mellitus as an indicator of physician compliance with clinical practice guidelines. Assessment of physician compliance with published guidelines may reveal areas of disagreement between physicians and guidelines or between physicians and patients and may show areas for potential improvement of care. Compliance with the diabetes care guidelines was assessed in our clinics to determine physician beliefs and performance and patients' accommodation of recommended practices. We interviewed 295 patients with diabetes and surveyed 47 providers at an academic family practice center to assess practices and beliefs regarding the care of patients with diabetes. We also reviewed a 1-year compilation of billing and referral records for physician use of glycosylated hemoglobin (hemoglobin A1c) testing and referral of patients for eye examinations. We found that physician beliefs and practices were divergent and that provider performance of these nationally recommended activities was low. More than 75% of providers said that they recommended hemoglobin A1c testing, but only about 50% of patients had a documented test in the billing system. When questioned, one third of the patients reported that their physicians recommended this test. Similarly, nearly all physicians stated that they recommended annual eye examinations, although only 43% of patients said that their primary care physician recommended this referral. Physicians can and must improve intervention and patient education in the care of diabetic patients. Patient knowledge, motivation, and practice must be augmented by physician

efforts. Lack of compliance with guidelines may indicate deficiencies in physician knowledge, implementation problems, lack of belief in guidelines, or problems in patient compliance. Attention should be directed to all these areas (Lawler &Viviani 1997).

2.6 Glycemic Control With Diet, Sulfonylurea, Metformin, or Insulin in Patients With Type 2 Diabetes Mellitus

Treatment with diet alone, insulin, sulfonylurea, or metformin is known to improve glycemia in patients with type 2 diabetes mellitus, but which treatment most frequently attains target fasting plasma glucose (FPG) concentration of less than 7.8 mmol/L (140 mg/dL) or glycosylated hemoglobin A_{1c}(HbA_{1c}) below 7% is unknown.obejective of this study is To assess how often each therapy can achieve the glycemic control target levels set by the American Diabetes Association. The proportion of patients who maintained target glycemic levels declined markedly over 9 years of follow-up. After 9 years of monotherapy with diet, insulin, or sulfonylurea, 8%, 42%, and 24%, respectively, achieved FPG levels of less than 7.8 mmol/L (140 mg/dL) and 9%, 28%, and 24% achieved HbA_{1c} levels below 7%. In obese patients randomized to metformin, 18% attained FPG levels of less than 7.8 mmol/L (140 mg/dL) and 13% attained HbA_{1c} levels below 7%. Patients less likely to achieve target levels were younger, more obese, or more hyperglycemic than other patients (American medical association 1999).

2.7 The hormone resistin links obesity to diabetes

Diabetes mellitus is a chronic disease that leads to complications including heart disease, stroke, kidney failure, blindness and nerve damage. Type 2 diabetes, characterized by target-tissue resistance to insulin, is epidemic in industrialized societies and is strongly associated with obesity; however, the mechanism by which increased adiposity causes insulin resistance is unclear. Here we show that adipocytes secrete a unique signalling molecule, which we have named resistin (for resistance to insulin). Circulating resistin levels are decreased by the anti-diabetic drug rosiglitazone, and increased in diet-induced and genetic forms of obesity. Administration of anti-resistin antibody improves blood sugar and insulin action in mice with diet-induced obesity. Moreover, treatment of normal mice with recombinant resistin impairs glucose tolerance and insulin action. Insulin-stimulated glucose uptake by adipocytes is enhanced by neutralization of

resistin and is reduced by resistin treatment. Resistin is thus a hormone that potentially links obesity to diabetes (steppan & savithabhat 2000).

2.8 Relative fracture risk in patients with diabetes mellitus, and the impact of insulin and oral antidiabetic medication on relative fracture risk

We studied the association between fractures and type 1 and type 2 diabetes mellitus. Type 1 and type 2 diabetes were associated with an increased risk (1) of any fracture (odds ratio [OR]=1.3, 95% CI: 1.2–1.5 for type 1 diabetes and 1.2, 95% CI: 1.1–1.3 for type 2 diabetes after adjustment for confounders) and (2) of hip fractures (OR=1.7, 95% CI: 1.3–2.2 for type 1 diabetes, and 1.4, 95% CI: 1.2–1.6 for type 2 diabetes). Furthermore, type 2 diabetes was associated with a significant increase in forearm fractures (OR=1.2, 95% CI: 1.0–1.5), and type 1 diabetes was associated with an increased risk of spine fractures (OR=2.5, 95% CI: 1.3–4.6), whereas type 2 diabetes was not. Use of metformin and sulphonylureas was associated with a significantly decreased risk of any fracture, whereas a non-significant trend towards decreased risk of any fracture was associated with the use of insulin. Except for a decrease in hip fractures with use of sulphonylureas, no change in fracture risk in the hip, spine or forearm was associated with the use of insulin or oral antidiabetic drugs (Diabetologia 2005).

2.9 The prevalence of retinopathy in the insulin-requiring diabetic patients of an English country town

A population-based survey of the insulin-requiring diabetics of a representative population was carried out. The overall prevalence of diabetes was 10.9/1000, that of insulin-requiring diabetes 4.1/1000. No retinopathy was found in 59%, background retinopathy was found in 33%and proliferative and advanced disease in 8%, diabetic maculopathy was present in 6.8% and the prevalence of potentially treatable disease undetected was 7.6%. Significant risk factors identified for retinopathy were increased duration of diabetes and elevated diastolic blood pressure, those for maculopathy an increased age at examination and onset of diabetes and an elevated systolic blood pressure (Mcleod & Rosentha 1988).

2.10 Lifestyle modification in management of diabetes mellitus.

India has the largest diabetic population in the world. Change in eating habits, increasing weight and decreased physical activity are major factors leading to increased incidence of type 2 diabetes. Obesity is the most important modifiable risk factor. Smoking is an independent risk factor for type 2 diabetes mellitus. Diet and exercise are primary therapeutic options for its management. Dietary management should not only aim to achieve glycaemic control but to normalize dyslipidaemia. Smoking cessation reduces the risk of morbidity and mortality in CAD. Exercise improves the condition of a diabetic patient. Exercise includes yoga practices which have a role to play in the prevention of type 2 diabetes (J Indian Med Assoc. 2002).

2.11 Global Prevalence of Diabetes Estimates for the year 2000 and projections for 2030

The goal of this study was to estimate the prevalence of diabetes and the number of people of all ages with diabetes for years 2000 and 2030. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The prevalence of diabetes is higher in men than women, but there are more women with diabetes than men. The urban population in developing countries is projected to double between 2000 and 2030. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people >65 years of age. These findings indicate that the "diabetes epidemic" will continue even if levels of obesity remain constant. Given the increasing prevalence of obesity, it is likely that these figures provide an underestimate of future diabetes prevalence (diabetes journals 1995).

2.12 Effect of Long-Term Monitoring of Glycosylated Hemoglobin Levels in Insulin-Dependent Diabetes Mellitus

The value of routine measurements of glycosylated hemoglobin (hemoglobin A_{1c}) in the care of patients with diabetes mellitus is uncertain. We undertook this study to determine whether knowledge of hemoglobin A_{1c} values would result in improved metabolic control in a group of patients with insulin-dependent diabetes mellitus (IDDM). Among the 222 patients still being

followed after one year, the mean hemoglobin A_{1c} value decreased significantly — from 10.1 to 9.5 percent ($P<0.005$) — in the group whose hemoglobin A_{1c} level was monitored ($n = 115$), whereas the initial and one-year values in the control group ($n = 107$) were 10.0 and 10.1 percent, respectively. The proportion of patients with poor control, defined as those having a hemoglobin A_{1c} value above 10.0 percent, decreased from 46 to 30 percent ($P<0.01$) in the group whose hemoglobin A_{1c} level was monitored but did not change significantly (45 to 50 percent) in the control group. The patients in the group whose hemoglobin A_{1c} level was monitored were seen and their insulin regimens changed more often, but they were hospitalized for acute care of their diabetes less often than those in the control group. A similar decrease in hemoglobin A_{1c} values occurred in the control group in the following year, when their care givers knew their hemoglobin A_{1c} values (mongens lykten & Horder 1990).

2.13 Phobia of self-injecting and self-testing in insulin-treated diabetes patients: opportunities for screening

It defines clinically relevant cut-off points for severe fear of self-injecting (FSI) and self-testing (FST) (phobia) in insulin-treated patients with diabetes, and to estimate the magnitude of these phobias in our research population. Seven patients participated in the self-injecting BAT: two patients refused to perform an extra injection. In the self-testing BAT ($n = 17$) four patients declined to perform the extra blood glucose self-test. Extrapolation of FSI and FST cut-off scores to the total research population showed that 0.2–1.3% of the population scored in the severe FSI range. In FST, 0.6–0.8% of the total study population obtained scores in the cut-off range. Severe FSI and FST, characterized by emotional distress and avoidance behaviour, seems to occur in a small group of insulin-treated patients with diabetes. The D-FISQ can be of use to health care professionals (physicians, nurse specialists) in quickly providing valuable information on levels of FSI and FST in diabetes patients (Mollema & snoek).

2.14 Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

There is no evidence from randomized trials to support a strategy of lowering systolic blood pressure below 135 to 140 mm Hg in persons with type 2 diabetes mellitus. We investigated whether therapy targeting normal systolic pressure (i.e., <120 mm Hg) reduces major

cardiovascular events in participants with type 2 diabetes at high risk for cardiovascular events. After 1 year, the mean systolic blood pressure was 119.3 mm Hg in the intensive-therapy group and 133.5 mm Hg in the standard-therapy group. The annual rate of the primary outcome was 1.87% in the intensive-therapy group and 2.09% in the standard-therapy group (hazard ratio with intensive therapy, 0.88; 95% confidence interval [CI], 0.73 to 1.06; P = 0.20). The annual rates of death from any cause were 1.28% and 1.19% in the two groups, respectively (hazard ratio, 1.07; 95% CI, 0.85 to 1.35; P = 0.55). The annual rates of stroke, a prespecified secondary outcome, were 0.32% and 0.53% in the two groups, respectively (hazard ratio, 0.59; 95% CI, 0.39 to 0.89; P = 0.01). Serious adverse events attributed to antihypertensive treatment occurred in 77 of the 2362 participants in the intensive-therapy group (3.3%) and 30 of the 2371 participants in the standard-therapy group (1.3%) (P <0.001) (Engl J. Med 2010).

2.15 Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes

Over 10 years, haemoglobin A_{1c} (HbA_{1c}) was 7·0% (6·2–8·2) in the intensive group compared with 7·9% (6·9–8·8) in the conventional group—an 11% reduction. There was no difference in HbA_{1c} among agents in the intensive group. Compared with the conventional group, the risk in the intensive group was 12% lower (95% CI 1–21, p=0·029) for any diabetes-related endpoint; 10% lower (−11 to 27, p=0·34) for any diabetes-related death; and 6% lower (−10 to 20, p=0·44) for all-cause mortality. Most of the risk reduction in the any diabetes-related aggregate endpoint was due to a 25% risk reduction (7–40, p=0·0099) in microvascular endpoints, including the need for retinal photocoagulation. There was no difference for any of the three aggregate endpoints between the three intensive agents (chlorpropamide, glibenclamide, or insulin).Patients in the intensive group had more hypoglycaemic episodes than those in the conventional group on both types of analysis (both p<0·0001). The rates of major hypoglycaemic episodes per year were 0·7% with conventional treatment, 1·0% with chlorpropamide, 1·4% with glibenclamide, and 1·8% with insulin. Weight gain was significantly higher in the intensive group (mean 2·9 kg) than in the conventional group (p<0·001), and patients assigned insulin had a greater gain in weight (4·0 kg) than those assigned chlorpropamide (2·6 kg) or glibenclamide (1·7 kg) (lancet 1998).

2.16 Evaluating Clinical Accuracy of Systems for Self-Monitoring of Blood Glucose

Although the scientific literature contains numerous reports of the statistical accuracy of systems for self-monitoring of blood glucose (SMBG), most of these studies determine accuracy in ways that may not be clinically useful. We have developed an error grid analysis (EGA), which describes the clinical accuracy of SMBG systems over the entire range of blood glucose values, taking into account 1) the absolute value of the system-generated glucose value, 2) the absolute value of the reference blood glucose value, 3) the relative difference between these two values, and 4) the clinical significance of this difference. The EGA of accuracy of five different reflectance meters (Eyetone, Dextrometer, Glucometer I, Glucometer II, Memory Glucometer II), a visually interpretable glucose reagent strip (Glucostix), and filter-paper spot glucose determinations is presented. In addition, reanalyses of a laboratory comparison of three reflectance meters (Accucheck II, Glucometer II, Glucoscan 9000) and of two previously published studies comparing the accuracy of five different reflectance meters with EGA is described. EGA provides the practitioner and the researcher with a clinically meaningful method for evaluating the accuracy of blood glucose values generated with various monitoring systems and for analyzinghttp://care.diabetesjournals.org/content/10/5/622.short the clinical implications of previously published data (William & Daniel Cox).

2.17 Glucose measurement in patients with diabetes mellitus with dermal interstitial fluid

Although measurement of capillary blood glucose remains the standard method of self-monitoring for persons with diabetes mellitus, a less-invasive method of monitoring would be desirable. Measurement of dermal interstitial fluid glucose might meet this need. To test this possibility, plasma glucose, capillary blood glucose (current standard), and dermal interstitial fluid glucose were measured in 17 subjects with type I diabetes during a 5-hour pre- and postprandial period when plasma glucose was changing rapidly. The objective was to assess the ability of dermal interstitial fluid glucose to accurately predict plasma glucose over a wide range of potential glucose concentrations. Dermal interstitial fluid glucose was highly correlated with plasma glucose (r = 0.95, $p < 0.0001$). The mean absolute and percent differences between dermal interstitial fluid glucose and plasma glucose were 1.2 mmol/L (21 mg/dl) and 10.6%, respectively. The kinetics of dermal interstitial fluid glucose and plasma glucose were similar. There was no significant difference between dermal interstitial fluid glucose and plasma glucose in mean glucose excursion,

peak glucose concentration, or time to peak glucose concentration. The correlation between dermal interstitial fluid glucose and plasma glucose was as strong as the correlation between capillary blood glucose and plasma glucose. In conclusion, dermal interstitial fluid glucose can be used to estimate plasma glucose, and has the potential to be used for monitoring patients with diabetes mellitus (john P Bantle 2000)

2.18 Approaches to Managing Hypoglycemia in Elderly Patients with Diabetes

Hypoglycemia is a common clinical problem in elderly patients with diabetes. Aging modifies the counterregulatory and symptomatic responses to hypoglycemia. Hypoglycemia in the elderly is not only due to tight blood sugar control, but also due to a multitude of other factors. Hypoglycemia often occurs with insulin, sulfonylureas, or meglitinide therapy. However, other causes may also contribute to hypoglycemia, such as decreased cognition, renal impairment, or polypharmacy. The presenting features of hypoglycemia may be atypical and misinterpreted, resulting in delayed treatment. Morbidity is greater in elderly patients, and the risk of progression to severe hypoglycemia is high because of their altered symptom profile, diminished symptom intensity, and altered glycemic thresholds. Hypoglycemia seems to be the main limiting factor in their glycemic Control (Diabetes association 1998).

2.19 Managing Hypoglycemia in Primary Care

Hypoglycemia is one of the most serious complications associated with glucose-lowering therapy and is a barrier to initiating, intensifying, and optimizing therapy, as well as long-term adherence.One survey found that, following a mild-to-moderate hypoglycemic episode, 74% of patients with type 1 diabetes mellitus (T1DM) (n = 202) and 43% with type 2 DM (T2DM) (n = 133) modified their insulin dose (FIgurE).Following a severe hypoglycemic episode, 78% and 58% of T1DM and T2DM patients, respectively, modified their insulin dose.The survey also found that two-thirds of patients consumed extra food to avoid a subsequent hypoglycemic episode. The consequences of hypoglycemia are numerous and include diminished patient psychological well-being and quality of life, fear and anxiety, and reduced productivity—the impact being greater following a severe hypoglycemic episode.For example, 29.9% of patients with T2DM were more fearful that a future hypoglycemic episode would occur following a mild or moderate hypoglycemic episode compared with 84.2% of patients following a severe hypoglycemic episode.Reports collected from a series of focus groups provide greater insight into the impact of

hypoglycemia on the daily lives of patients with T1DM or T2DM (N = 18) (pimary care education consortium 2012).

2.20 A Review of the Challenge in Measuring Hemoglobin A1c

The attraction of the simple biochemical concept combined with a clinical requirement for a long-term marker of glycolic control in diabetes has made hemoglobin A1c (HbA1c) one of the most important assays undertaken in the medical laboratory. The diversity in the biochemistry of glycation, clinical requirements, and management demands has resulted in a broad range of methods being developed since HbA1c was described in the late 1960s. A range of analytic principles are used for the measurement of HbA1c. The charge difference between hemoglobin A0 and HbA1c has been widely utilized to separate these two fractions, most notably found these days in ion-exchange high-performance liquid chromatography systems; the difference in molecular structure (affinity chromatography and immunochemical methods) are becoming widely available. Different results found in different laboratories using a variety of HbA1c analyses resulted in the need for standardization, most notably in the United States, Japan, and Sweden. Designated comparison methods are now located in these three countries, but as they are arbitrarily chosen and have differences in specificity, results of these methods and the reference values and action limits of the methods differ and only harmonized HbA1c in specific geographic areas. A reference measurement system within the concept of metrological traceability is now globally accepted as the only valid analytic anchor. However, there is still discussion over the units to be reported. The consensus statement of the International Federation of Clinical Chemistry (IFCC), the American Diabetes Association, the International Diabetes Federation, and the European Association for the Study of Diabetes suggests reporting HbA1c in IFCC units (mmol/mo), National Glycohemoglobin Standardization Program units (%), and estimated average glucose (either in mg/dl or mmol/liter). The implementation of this consensus statement raised new questions, to be answered in a concerted action of clinicians, biochemists, external quality assessment organizers, patient groups, and manufacturers (CAS Weykamp).

2.21 Weight Control Practices and Disordered Eating Behaviors Among Adolescent Females and Males With Type 1 Diabetes

This study examines the prevalence of specific weight control practices/disordered eating behaviors and associations with sociodemographic characteristics, BMI and weight perceptions, family functioning, and metabolic control among adolescent females and males with type 1 diabetesUnhealthy weight control practices were reported by 37.9% of the females and by 15.9% of the males. Among the females, 10.3% reported skipping insulin and 7.4% reported taking less insulin to control their weight. Only one male reported doing either of these behaviors. Weight control/disordered eating behaviors were not associated with age, parental level of education, family structure, or race/ethnicity. Higher levels of weight dissatisfaction tended to be associated with unhealthy weight control/disordered eating; associations with BMI were inconsistent. Family cohesion was negatively associated with disordered eating among females ($r = -0.52$; $P < 0.001$) and males ($r = -0.41$; $P < 0.001$), but correlations with other measures of family environment (control, independence, and responsibility for diabetes management) were not significant. Correlations between disordered eating and HbA1c levels were significant among females ($r = 0.33$; $P < 0.01$) and males ($r = 0.26$; $P < 0.05$) (Dianne & neumark).

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2.22 Knowledge and practice of foot care in people with diabetes

To determine knowledge and practice of foot care in people with diabetes a questionnaire was completed by patients in Middlesbrough, South Tees, UK. A knowledge score was calculated and current practice determined. Practices that put patients at risk of developing foot ulcers and barriers to good practice were identified. Patients at high risk of ulceration were compared to those at low risk. The mean knowledge score was 6.5 (S.D. 2.1) out of a possible 11. There was a positive correlation between the score and having received advice on foot care (6.9 versus 5.4, P=0.001). Deficiencies in knowledge included the inability to sense minor injury to the feet (47.3%), proneness to ulceration (52.4%) and effect of smoking on the circulation (44.5%). 24.6% (20.1–29.2) never visited a chiropodist, 18.5% (14.2–22.7) failed to inspect their feet and 83% (79.1–86.9) did not have their feet measured when they last purchased shoes. Practices that put patients at risk included use of direct forms of heat on the feet and walking barefoot. Barriers to practice of foot care were mainly due to co-morbidity. Those with high risk feet showed a higher (6.8) but not significant knowledge score compared to those at low risk (6.5) and their foot care practise was

better. The highlight areas where efforts to improve knowledge and practice may contribute to the prevention of foot ulcers and amputation (Pollack & Connolly 2003).

2.23 Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes

Determine whether tight control of blood pressure prevents macrovascular and microvascular complications in patients with type 2 diabetes. Mean blood pressure during follow up was significantly reduced in the group assigned tight blood pressure control (144/82 mm Hg) compared with the group assigned to less tight control (154/87 mm Hg) ($P<0.0001$). Reductions in risk in the group assigned to tight control compared with that assigned to less tight control were 24% in diabetes related end points (95% confidence interval 8% to 38%) (P=0.0046), 32% in deaths related to diabetes (6% to 51%) (P=0.019), 44% in strokes (11% to 65%) (P=0.013), and 37% in microvascular end points (11% to 56%) (P=0.0092), predominantly owing to a reduced risk of retinal photocoagulation. There was a non-significant reduction in all cause mortality. After nine years of follow up the group assigned to tight blood pressure control also had a 34% reduction in risk in the proportion of patients with deterioration of retinopathy by two steps (99% confidence interval 11% to 50%) (P=0.0004) and a 47% reduced risk (7% to 70%) (P=0.004) of deterioration in visual acuity by three lines of the early treatment of diabetic retinopathy study (ETDRS) chart. After nine years of follow up 29% of patients in the group assigned to tight control required three or more treatments to lower blood pressure to achieve target blood pressures (US national library of medicine n national institute of health 1998).

2.24 Inpatient management of diabetes and hyperglycemia among general medicine patients at a large teaching hospital

Determine the current state of glucose management on an academic hospitalist service and the relationship between insulin-ordering practices and glycemic control. The mean rate of hyperglycemia was 31% of measurements per patient. Basal insulin was ordered for 43% of patients, and scheduled rapid- or short-acting insulin was ordered for 4% of patients. Sixty-five percent of patients who had at least 1 episode of hyper- or hypoglycemia had no change made to any insulin order during the first 5 days of the hospitalization. When adjusted for clinical factors, the use of sliding-scale insulin by itself was associated with a 20 mg/dL higher mean glucose level per patient-day (Schnipper, Barsky et. al 2006).

3.1 Significance of the study:

Diabetes mellitus is a chronic metabolic disease with a large number of complications that cause a huge burden of morbidity. The emphasis in diabetes care often focuses on vascular and neuropathic complications and there is evidence that this approach is starting to impact on the incidence of complications.(singh and Hunter 2006)(R Singh , J Hunter, C Fulton Practical Diabetes International Volume 23, Issue 6, Article first published online: 3 AUG 2006) Diabetics cannot sufficiently utilise carbohydrates such as sugar, which is an important energy source. Insulin plays a significant role here as it is a blood-sugar reducing endogenous hormone and the production of insulin is lower in those affected. Furthermore, the cells in their bodies are not able to properly absorb the insulin that is available. The reason for this is the highly diminished sensitivity of the cells towards insulin. The cell membranes are unable to recognise the hormone and therefore do not absorb enough of it. The consequence of this so-called insulin resistance is that not enough energy is produced in the cells.(mohan & Das 1998)Diabetes mellitus is a complex, chronic illness requiring continuous medical care with multifactorial risk reduction strategies beyond glycemic control. Ongoing patient self-management education and support are critical to preventing acute complications and reducing the risk of long-term complications. Significant evidence exists that supports a range of interventions to improve diabetes outcomes. (American Diabetes Association)In Bangladesh percentage of diabetes is increasing at alarming rate.in this regard we conducted a survey among 202 diabetes patient in Dhaka to know the the proper diabetes care, practice they take to control diabetes and their treatment plan.

3.2 The objective of the study:

- To know measures of people taken to control diabetes and their practices.
- Can also know the proper treatment plan,medicines,various test taken to measure the diabetes.

4.1 Type of study

The study was a survey based study.

4.2 Study area

The study was done in BIRDEM, the Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders at Shahbag, Dhaka. BIRDEMat rampura,Dhaka and chondrima uddan(sangshad vaban) park.

4.3 Study population

The survey was performed on 202 diabetic patients.

Inclusion criteria

In this survey, only Diabetic patients were included.

Exclusion criteria

In this survey, children and pregnant women was not added in the survey.

4.4 Questionnaire development

The questionnaire was developed on the basis of some criteria that influence the proper parctice and treatment of people. It is done on basis of Bangladesh social environment to collect maximum information and data about practice and treatment of diabetes.

4.5 Procedure:

We had done survey among 202 diabetes patient both male and female and developed questionnaires and collected data about their daily treatment and practice.

4.6 Data analysis:

We analysis our data by using Microsoft excel.

5.1 Socio-demographic data:

Table 5.1: Socio-demographic data table

Variables		n (%)
Sex	Male	105(51.44%)
	Female	97(51.44%)
Marital status	Single	8(3.96%)
	Married	194(96.53%)
	Divorced	0
Level of education	Illiterate	56(27.4%)
	Primary	62(30.29%)
	Secondary	31(15.18%)
	College	29(14.9%)
	Graduate	18(9.13%)
	Post graduate	6(3.1%)
Age	<40	14(6.73%)
	40-50	137(68.26%)
	>60	43(21.51%)
Family income	<5000	2(0.96%)
	5000-6000	7(3.36%)
	10000-25000	56(27.88%)
	>25000	36(17.78)
Living with family	yes	92(45.67%)
	No	8(3.85%)
Major type of diabetes	1	3(1.92%)
	2	24(12.02%)
	3	23(11.54%)
	4	17(8.65%)
	Don’t know	127(62.98%)
Type of diabetes mellitus	Type-1	16(8.17%)

	Type-2	10(4.8%)
	Don’t know	162(80.29%)
Duration Of Diabetes mellitus	<1 year	13(6.73%)
	1.1-1.5	48(24.03%)
	5.1-10	81(39.9%)
	10.1-20	46(22.59%)
	>20	8(3.84%)
Mode of diagnosis	Symptomatic	117(57.21%)
	Incidental	85(39.9%)
Family history of diabetes	Yes	92(45.02%)
	No	78(38.46%)
	Don’t know	30(14.42%)

5.2 Frequency of visiting healthcare provider

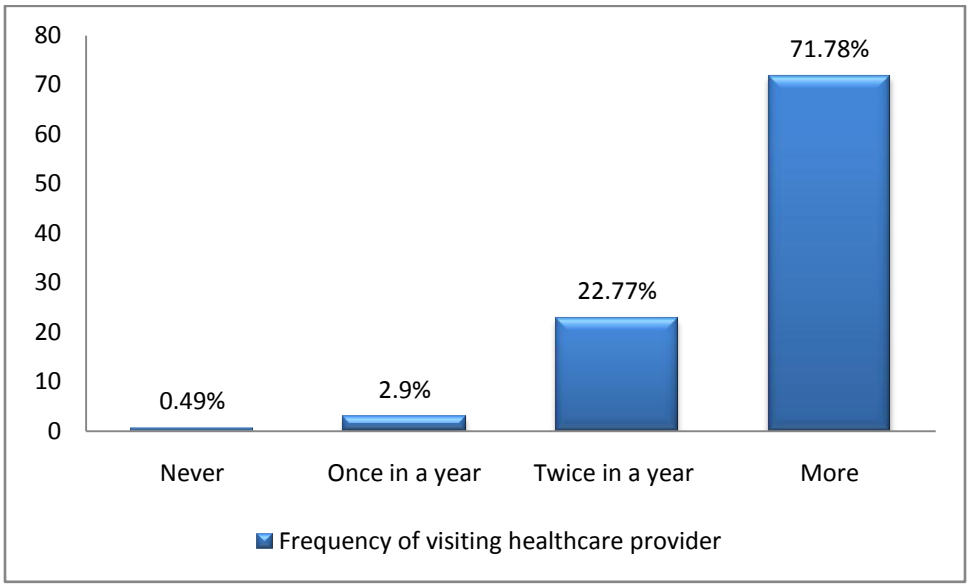

Figure 5.1: Frequency of visiting healthcare provider

5.3 Knowledge about normal range of fasting blood glucose level

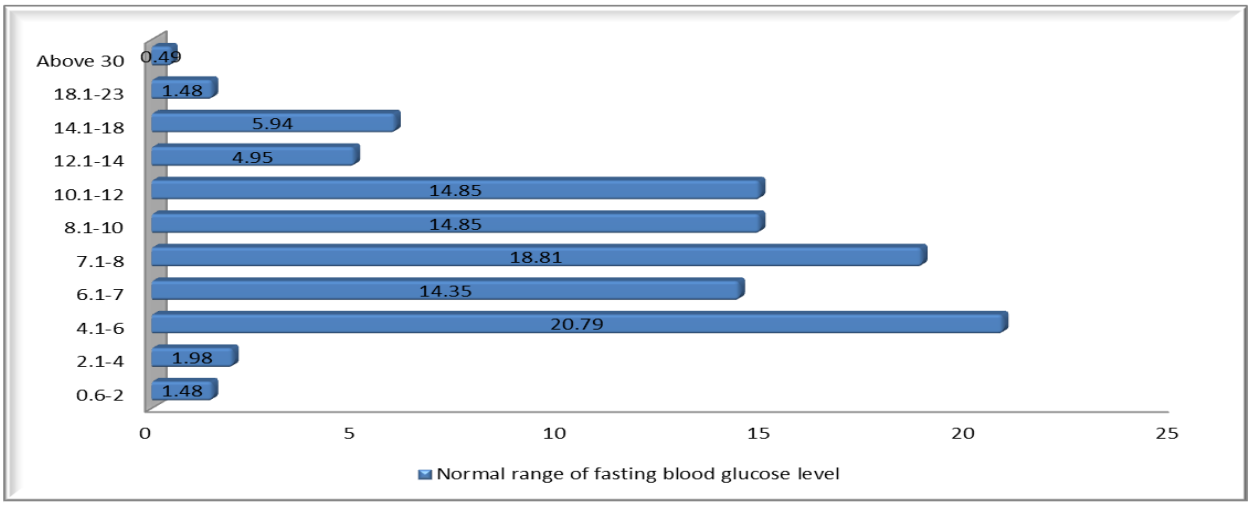

Figure 5.2: Knowledge about normal range of fasting blood glucose level

5.4 Knowledge about normal range of random blood glucose level

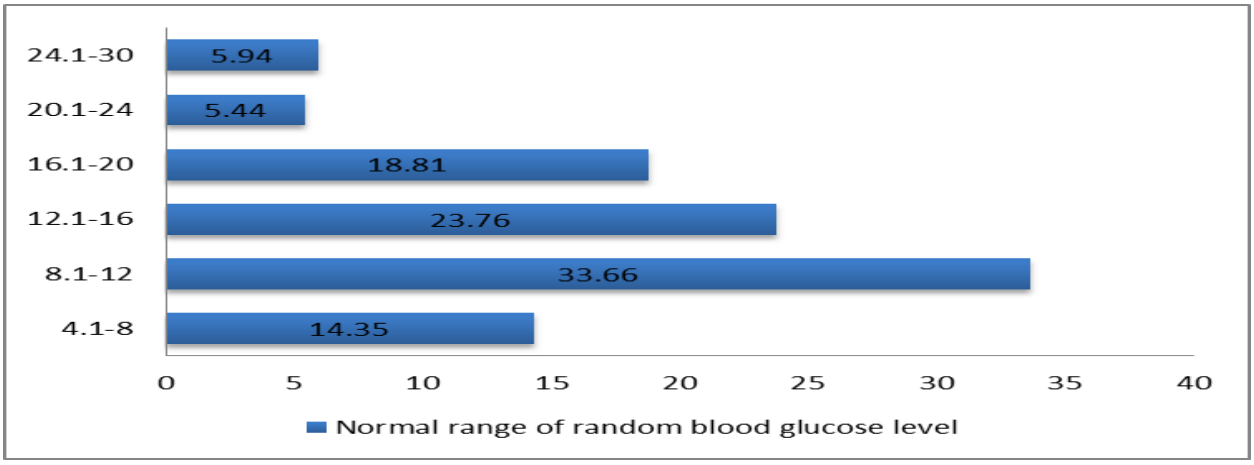

Figure 5.3: Knowledge about normal range of random blood glucose level

5.5 steps taken to manage hyperglycemia

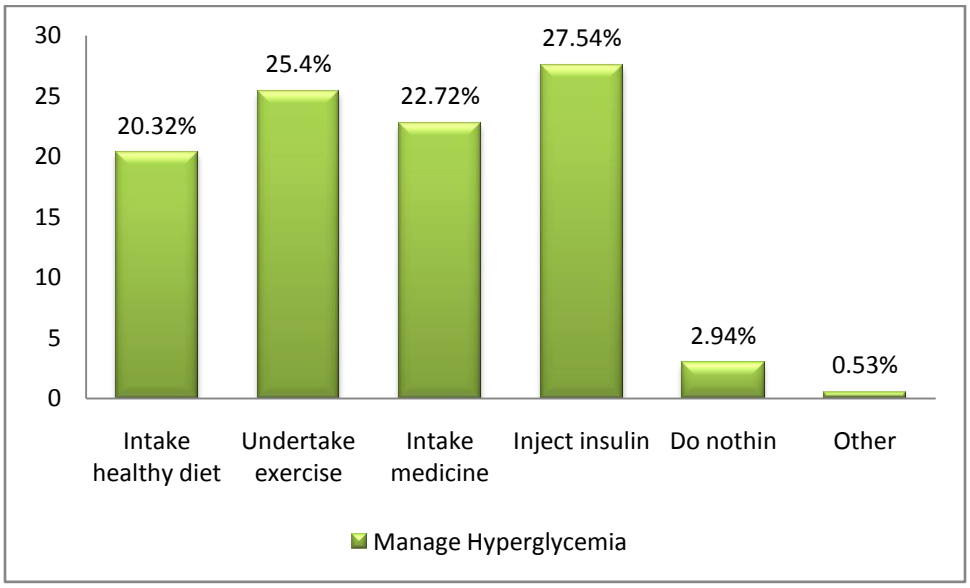

Figure 5.4: steps taken to manage hyperglycemia

5.6 Steps taken to manage hypoglycemia

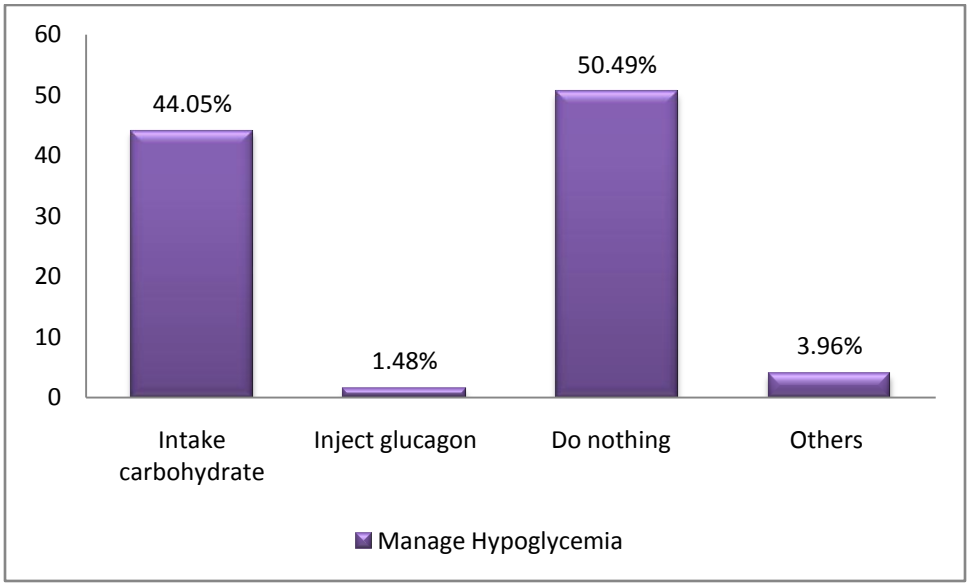

Figure 5.5: Steps taken to manage hypoglycemia

5.7 sources of DM knowledge

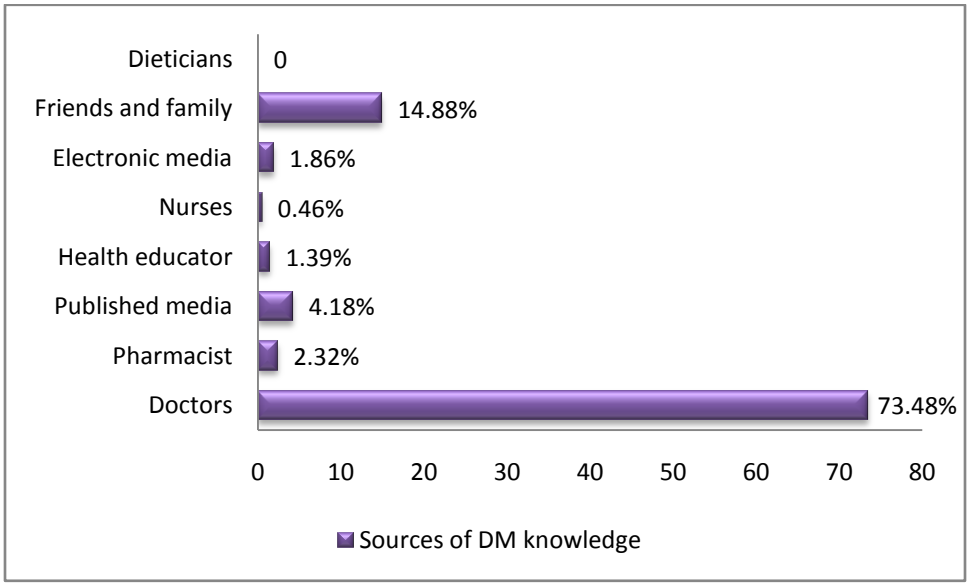

Figure 5.6: sources of DM knowledge

5.8 Performed Glycated hemoglobin or HbA1c test

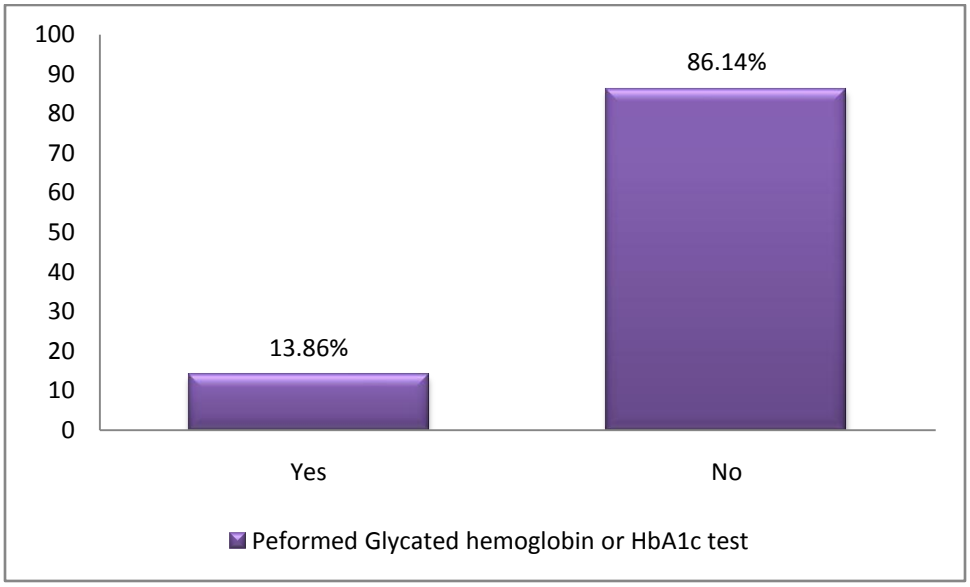

Figure 5.7: Performed Glycated hemoglobin or HbA1c test

5.9 Visiting frequency of DM clinic/doctor for follow up

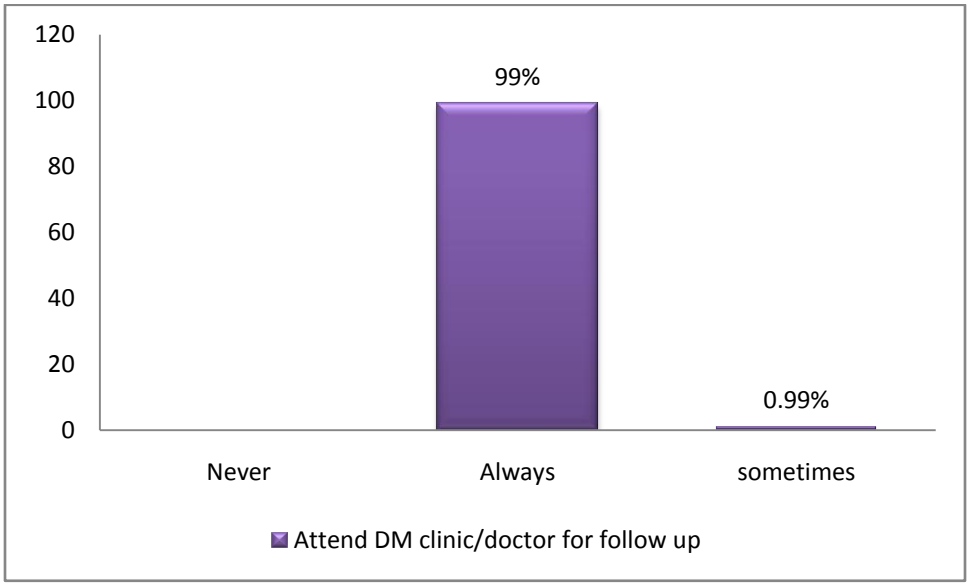

Figure 5.8: Visiting frequency of DM clinic/doctor for follow up

5.10 Frequency of controlling weight

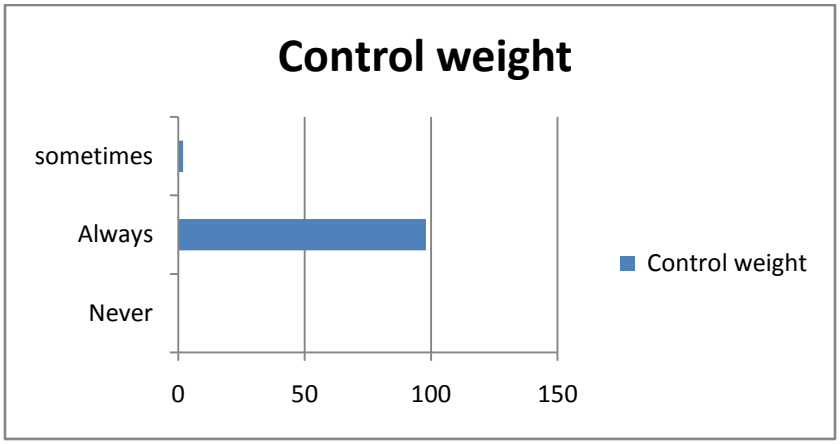

Figure 5.9: Frequency of controlling weight

5.11 Frequency of undertaking physical exercise

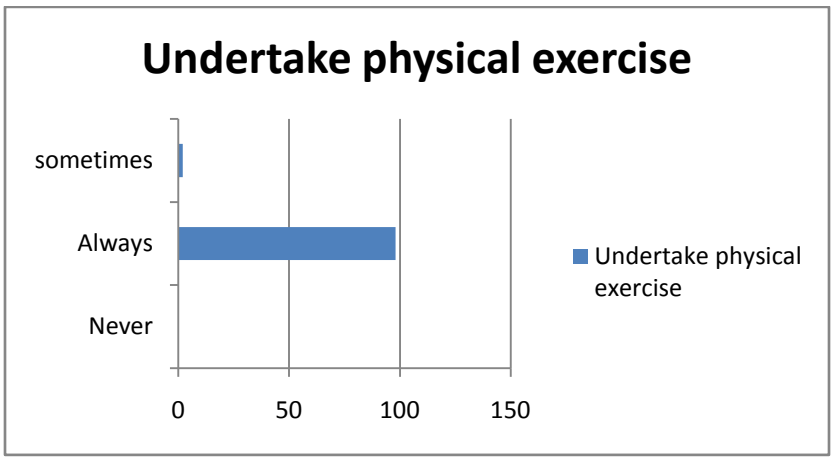

Figure 5.10: Frequency of undertaking physical exercise

5.12 Frequency of following special diet

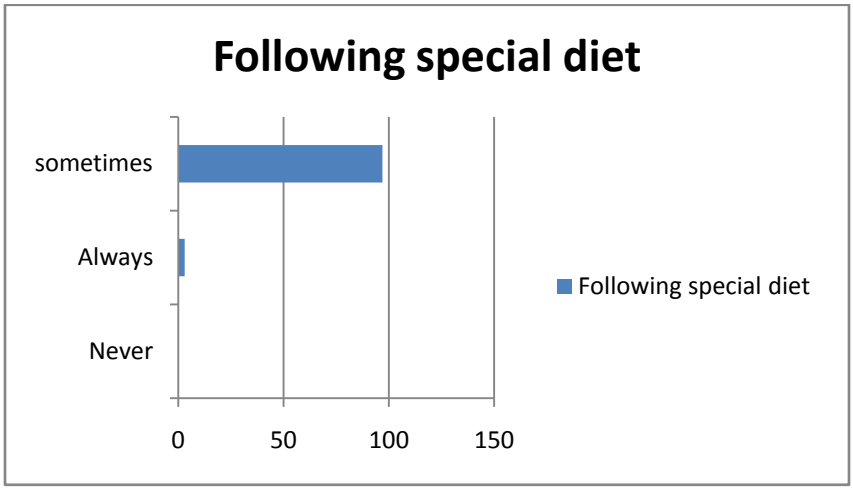

Figure 5.11: Frequency of following special diet

5.13 Frequency of Complying with medication

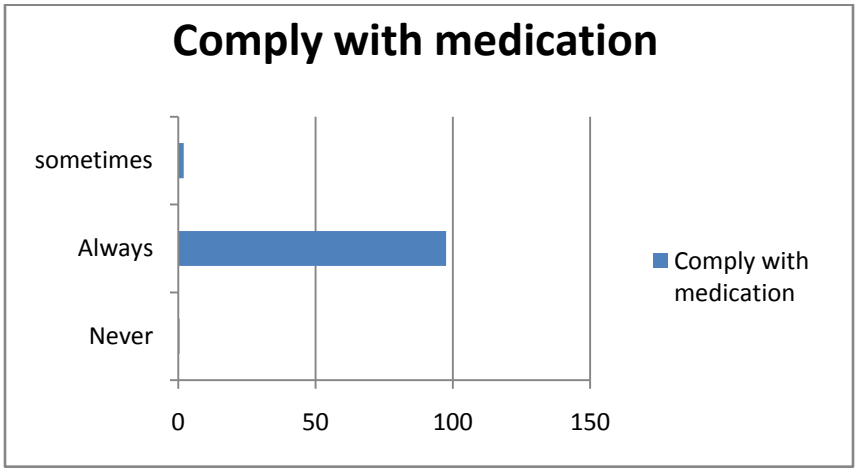

Figure 5.12: Frequency of Complying with medication

5.14 Frequency of Taking care of toes and feet

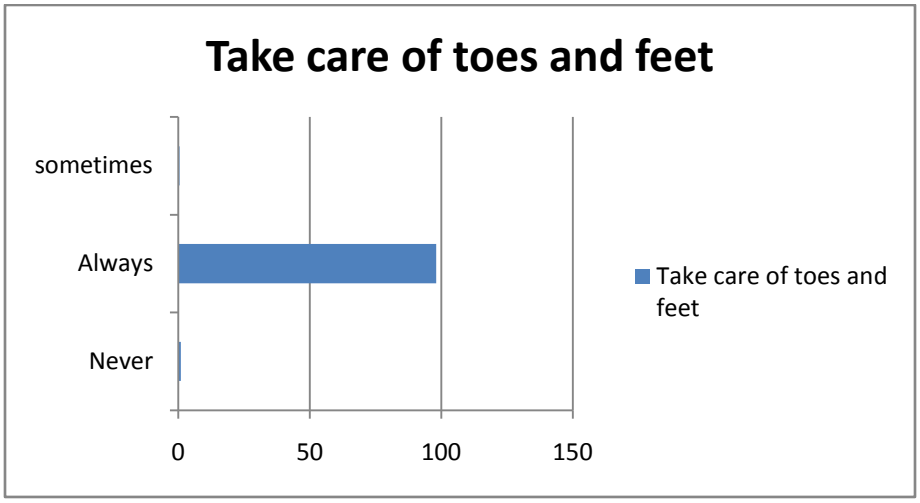

Figure 5.13: Frequency of Taking care of toes and feet

5.15Frequency of checking blood pressure

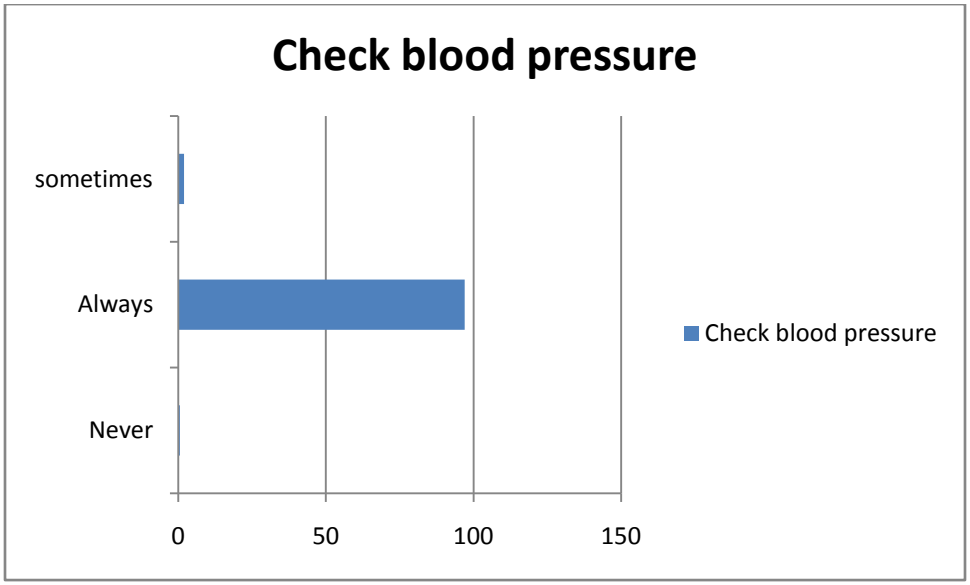

Figure 5.14: Frequency of checking blood pressure

5.16 Frequency of checking lipid profile

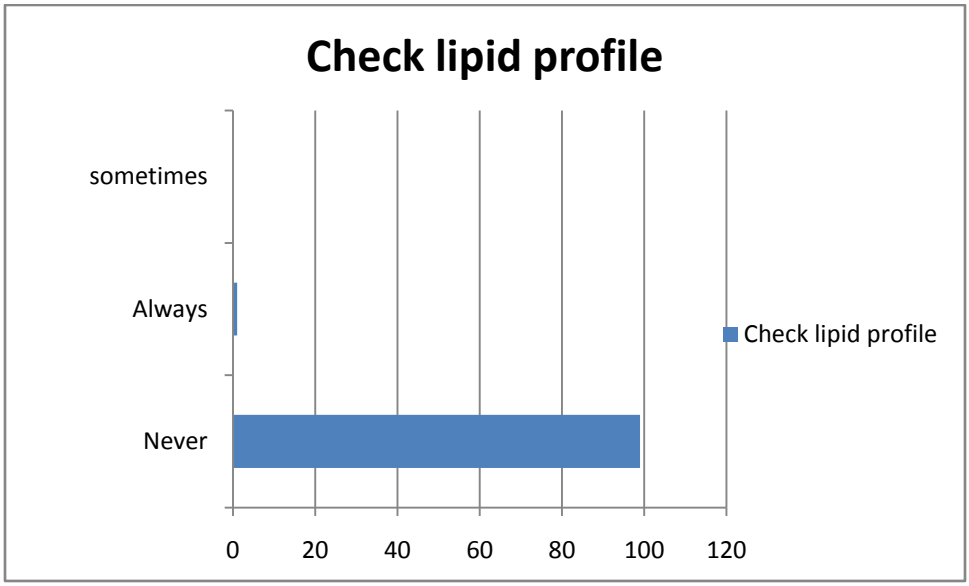

Figure 5.15: Frequency of checking lipid profile

5.17Frequency of performing urine examination

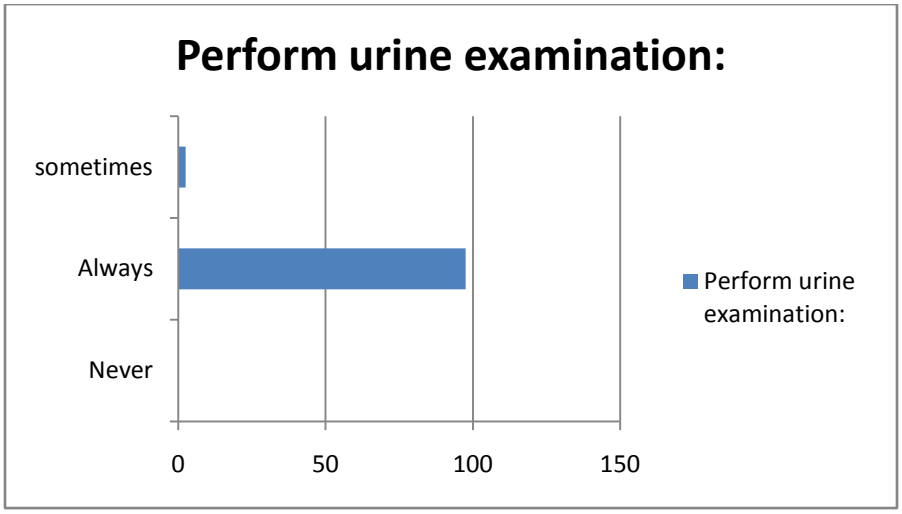

Figure 5.16: Frequency of performing urine examination

5.18 Frequency of check blood glucose level

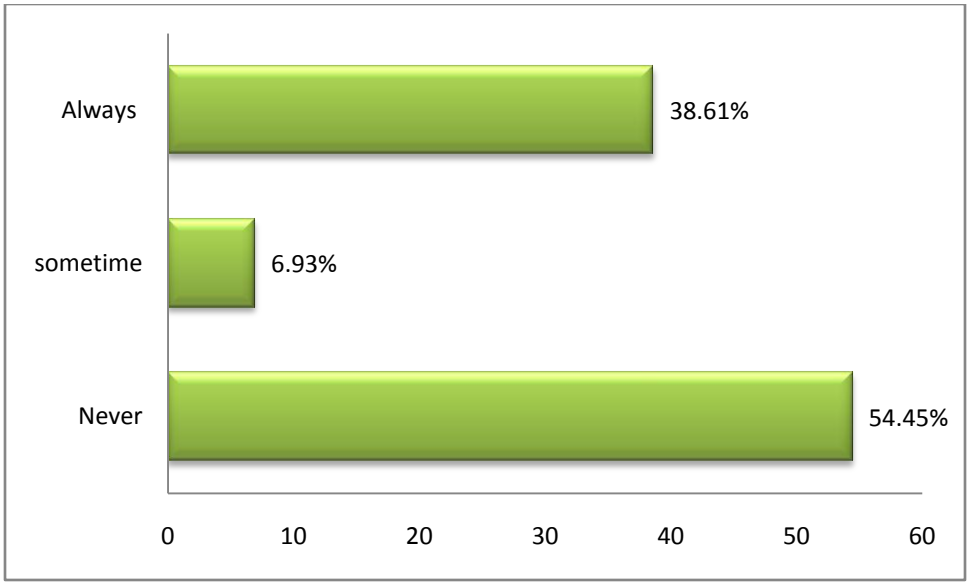

Figure 5.17: Frequency of check blood glucose level

5.19 Conception about most accurate method of monitoring Diabetes

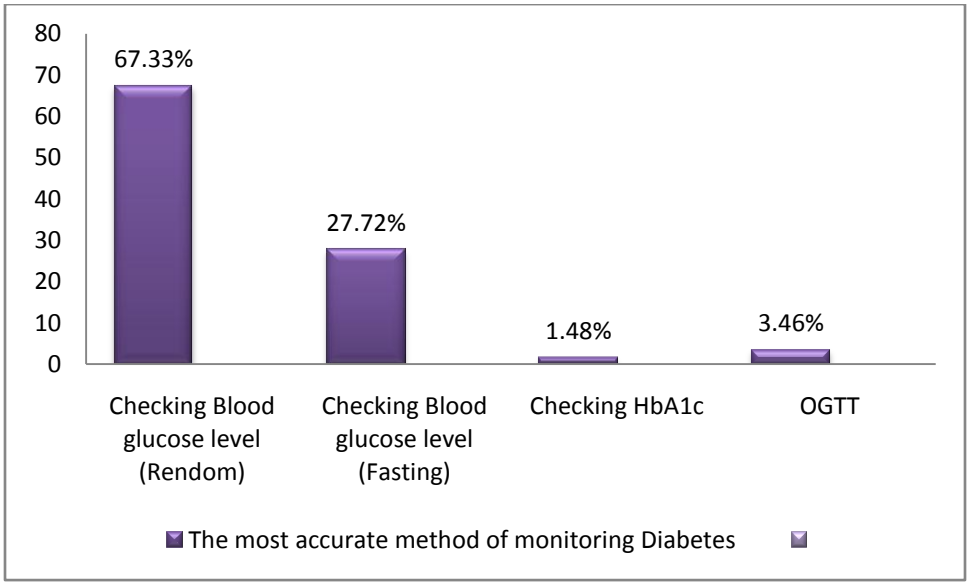

Figure 5.18: Conception about most accurate method of monitoring Diabetes

5.20 Frequency of patients self testing of blood sugar

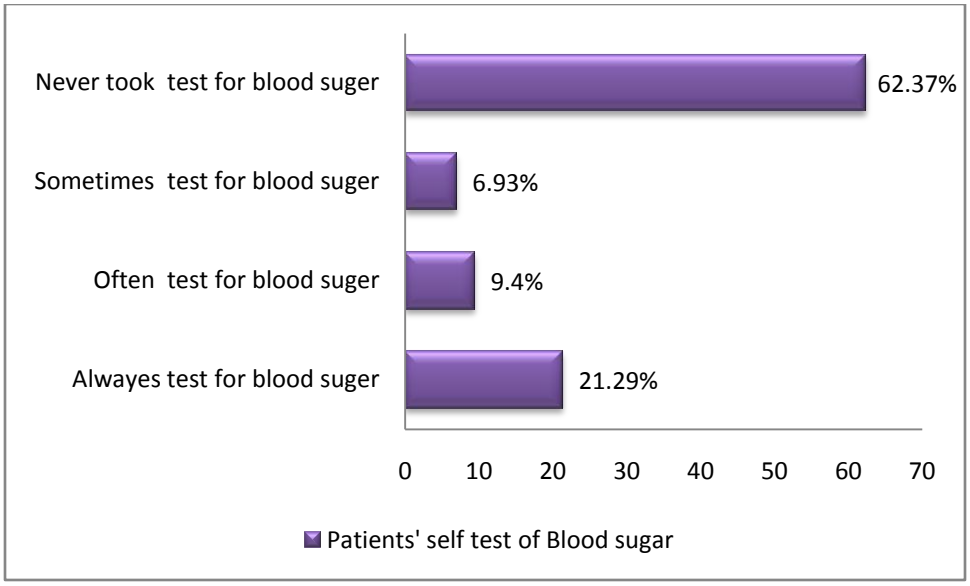

Figure 5.19: Frequency of patients self testing of blood sugar

5.21patients self control of blood sugar

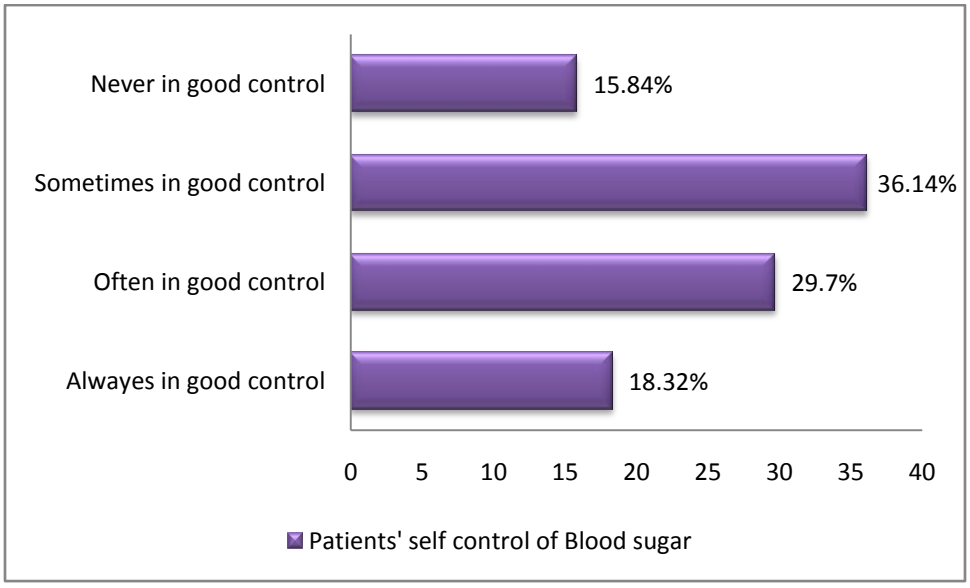

Figure 5.20: patients self control of blood sugar

5.22 Barriers of self testing

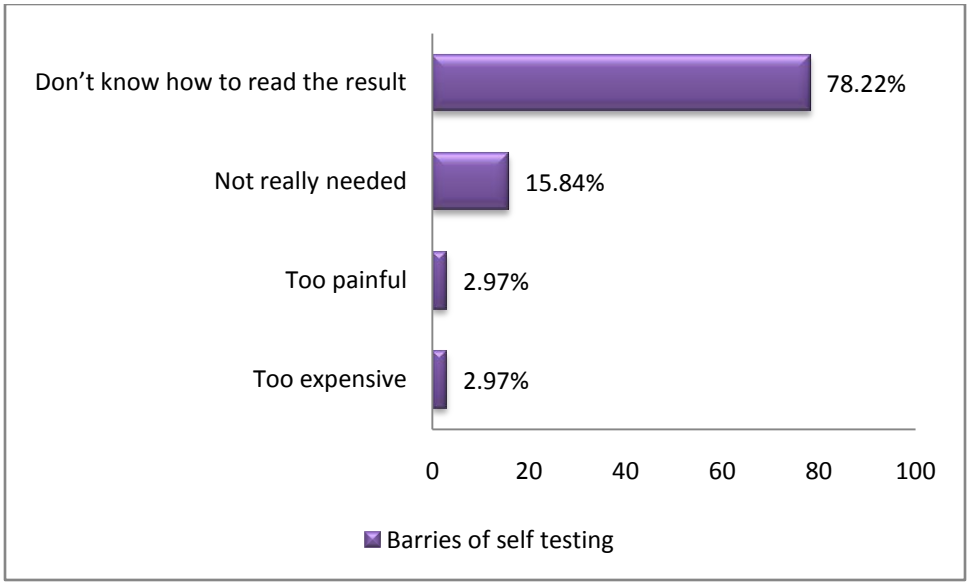

Figure 5.21: Barriers of self testing

5.23 Idea about keep in touch with physicians

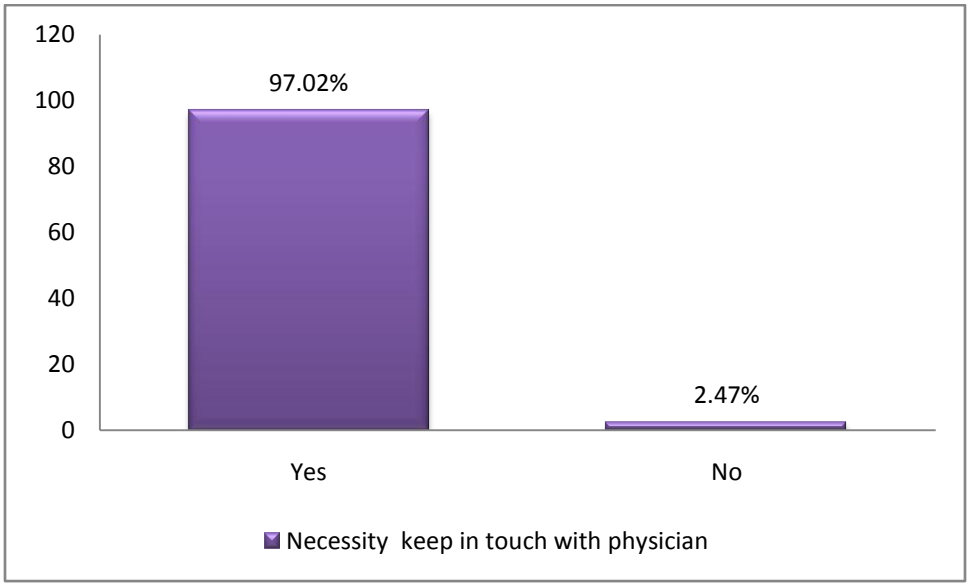

Figure 5.22: Idea about keep in touch with physicians

5.24 Conception about negative effect of missing dose

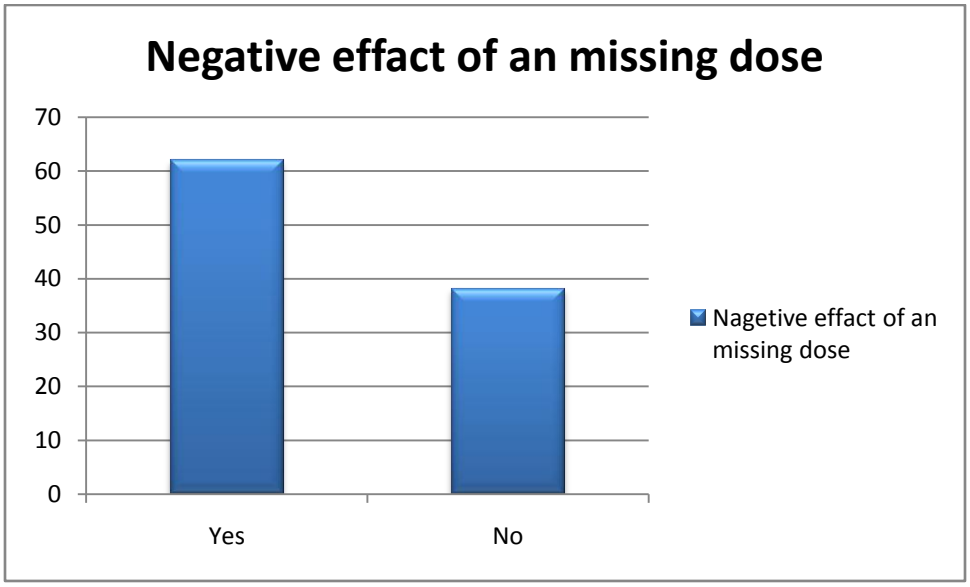

Figure 5.23: Conception about negative effect of missing dose

5.25 Patient taking medication to control diabetes

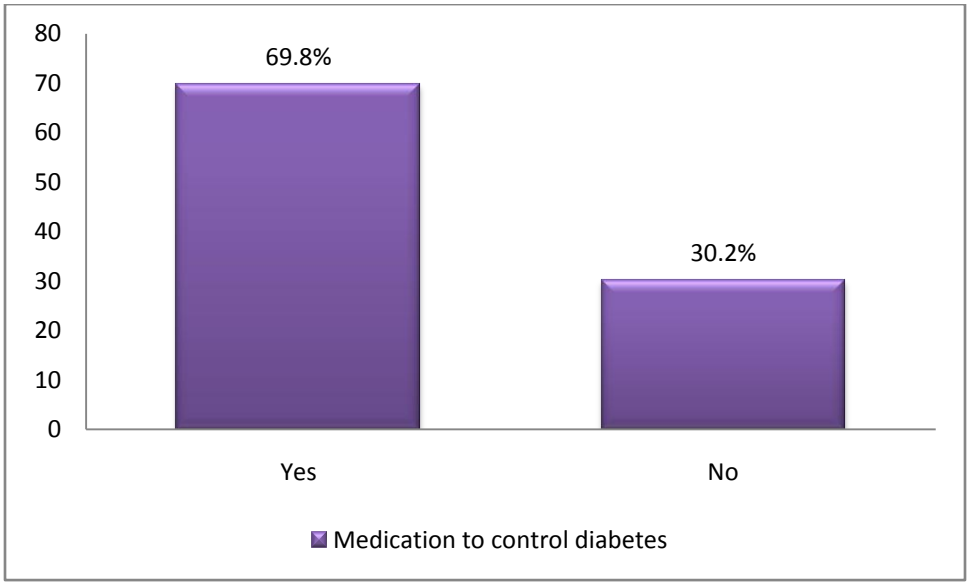

Figure 5.24: Patient taking medication to control diabetes

5.26 Type of medication prescribed by physicians

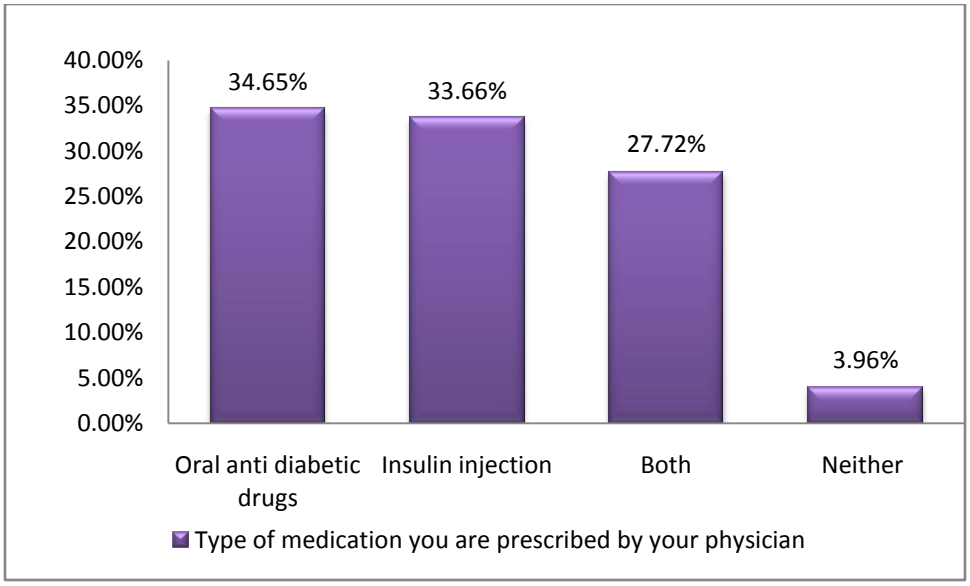

Figure 5.25: Type of medication prescribed by physicians

5.27 Medications prescribed for DM

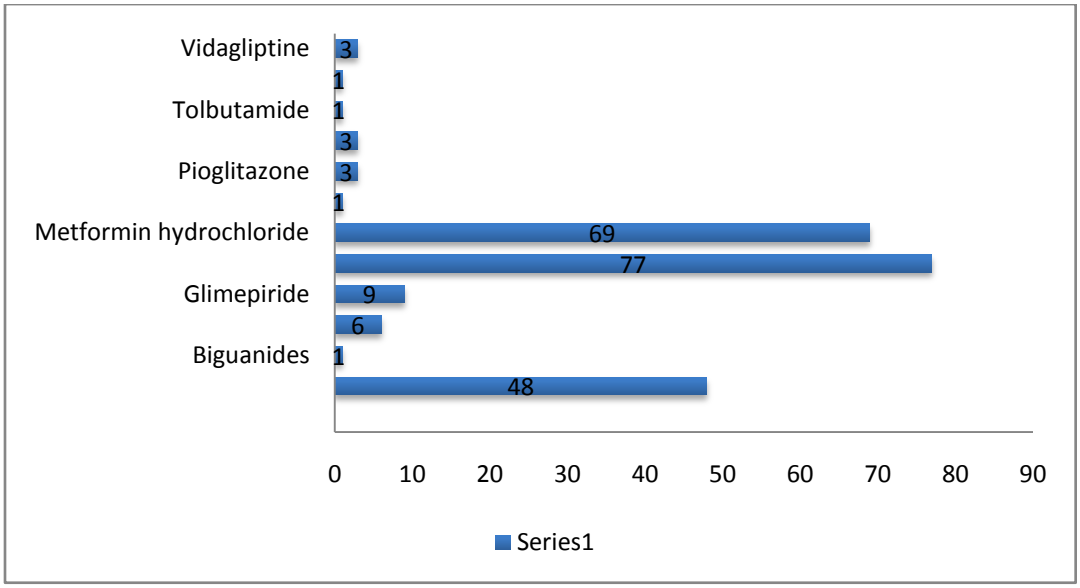

Figure 5.26: medications prescribed for DM

6.1 Dicussion:

According to Mahajan, korrane et al. One hundred consecutive diabetes mellitus patients attending the diabetic clinic of the hospital constituted the study group. One hundred age and sex matched non-diabetics were taken as controls. The majority, 63%, belonged to the 41-60 years age group and 98% had non-insulin dependent diabetes.

In the present study among 202 diabetic patients 51.44% male and 48.55% female. Patients were selected randomly in this survey. It was considered factors affecting diabetes knowledge were sex, age, and level of education, marital status, profession, and income, mode of diagnosis and duration of diabetes. Interestingly, analysis showed a positive correlation between patients' knowledge and the number of contacts with a diabetic education in the last two years. Only Diabetic patients were selected as study population. 96.53% of them were married and 3.96% were single. In the basis of level of education most of the populations were received Primary (30.29%) education Illiterate (27.4%) some of them were received secondary (15.18%),College(14.9%),Graduate (9.13%),post graduate(3.1%). Among of those study population age below 40 diabetic patients 6.73%, age between 40-50 (68.26%) and more than 60 (21.51%).some of them live with family is about 45.67% and don't live with family of about 3.85%.It is also observed duration of action of diabetes. Among them highest population suffer their diabetes of about 1.1-1.5 year. On the other hand lowest percentage of people of about 3.84% suffers from diabetes greater than 20 years. Family history is another important factor where 45.02% having family diabetes, 38.46% of population don't have family diabetes .On the other hand 14.42% of people don't know about their family history of diabetes. (Table-5.1)

Hypoglycemia is one of the most serious complications associated with glucose-lowering therapy and is a barrier to initiating, intensifying, and optimizing therapy, as well as long-term adherence.Acoording to primary care of education consortium to moderate hypoglycemic episode, 74% of patients with type 1 diabetes mellitus (T1DM) (n = 202) and 43% with type 2 DM (T2DM) (n = 133) modified their insulin dose. They followed a severe 78% of type 1 diabetes patient and 58% of type 2 diabetes patient take modified insulin dose ,they also found that two third of this population consumed extra food to lower their hypoglycemic period.

Moreover in our survey it is found that, among 202 diabetic patients including male and female groups in case of hypoglycemia 44.05% of population intake carbohydrate, 1.48% of population inject glucagon, 3.96% of people take other steps to prevent hypoglycemia. Huge population of about 50.49% does nothing to control their hypoglycemia. (Figure-5.5)

According to Weykamp, W. Garry John and Mosca glycolic control in diabetes has made hemoglobin A1C (HbA1c) one of the most important assays undertaken in the medical laboratory. Different results found in different laboratories using a variety of HbA1c analyses resulted in the need for standardization, most notably in the United States, Japan, and Sweden. International Federation of Clinical Chemistry (IFCC), the American Diabetes Association, the International Diabetes Federation, and the European Association for the Study of Diabetes suggests reporting HbA1c in IFCC units (mmol/mo),National Glycohemoglobin Standardization Program units (%), and estimated average glucose (either in mg/dl or mmol/liter).

In the present study on practice and treatment of diabetes mellitus incase of determination of diabetes mellitus hbA1c test is not so popular among the patients. The test is performed among 202 men and women .Between them only 13.86% of the population know about performed hbA1c test and majority of them 86.14% don’t have any idea about the test.(Figure-5.7)

Patterson, Mellin et al studied that the prevalence of specific weight control practices/disordered eating behaviors and associations with socio demographic characteristics, BMI and weight perceptions, family functioning, and metabolic control among adolescent females and males with type 1 diabetes Unhealthy weight control practices were reported by 37.9% of the females and by 15.9% of the males. Among the females, 10.3% reported skipping insulin and 7.4% reported taking less insulin to control their weight.

In the study shows that in controlling diabetes mellitus both types(type 1 and 2) maintaining a standard weight is thought to be very important.98.01% people control their weight and remaining 1.96% people control their weight not in regular basis.(Figure-4.9)

According to Pollock, Unwin et al. a questionnaire was completed by patients in Middlesbrough, South Tees, UK. A knowledge score was calculated and current practice

determined. Practices that put patients at risk of developing foot ulcers and barriers to good practice were identified. Patients at high risk of ulceration were compared to those at low risk. The mean knowledge score was 6.5 (S.D. 2.1) out of a possible 11. There was a positive correlation between the score and having received advice on foot care (6.9 versus 5.4, P=0.001).

In this study of practicing of taking care of foot and toes 98.01% of total population take care their foot and toes and very minor population only about a 0.99% people never take care their foot and toes.(Figure-5.13)

Us national library of medicine and national institute of health study shows that Mean blood pressure during follow up was significantly reduced in the group assigned tight blood pressure control (144/82 mm Hg) compared with the group assigned to less tight control (154/87 mm Hg). Reductions in risk in the group assigned to tight control compared with that assigned to less tight control were 24% in diabetes related end points (95% confidence interval 8% to 38%) (P=0.0046), 32% in deaths related to diabetes (6% to 51%) (P=0.019), 44% in strokes (11% to 65%) (P=0.013), and 37% in micro vascular end points (11% to 56%) (P=0.0092),.

On the other hand the study shows that 97.02% of the total population controls their blood pressure and 1.98% of the people sometimes control their blood pressure. (Figure-5.14)

Bantle and Thomas study showed that with type I diabetes during a 5-hour pre- and postprandial period when plasma glucose was changing rapidly. The objective was to assess the ability of dermal interstitial fluid glucose to accurately predict plasma glucose over a wide range of potential glucose concentrations. Dermal interstitial fluid glucose was highly correlated with plasma glucose ($r = 0.95, p < 0.0001$). The mean absolute and percent differences between dermal interstitial fluid glucose and plasma glucose were 1.2 mmol/L (21 mg/dl) and 10.6%, respectively

On the other hand 38.61%people always check blood glucose level to control diabetes 6.93% among them check sometimes but majority of the people never check their glucose level regularly of about.54.45 %.(Figure-5.17)

Clarke, Cox et.al study shows that statistical accuracy of systems for self-monitoring of blood glucose (SMBG), most of these studies determine accuracy in ways that may not be clinically useful. They have developed an error grid analysis (EGA), which describes the clinical accuracy of SMBG systems over the entire range of blood glucose values. The EGA of accuracy of five different reflectance meters (Eyetone, Dextrometer, Glucometer I, Glucometer II, Memory Glucometer II), a visually interpretable glucose reagent strip (Glucostix), and filter-paper spot glucose determinations is presented.

But present study shows that patients self test of checking blood sugar is not very popular 62.37% among them never took self test ,6.93% sometimes check blood sugar 9.4% ,often check blood sugar and 21.29% of the whole population always check their blood sugar on their own. The barrier of their self testing is also not up to the mark 78.22% among them don't know how to read result and 15.84% of the population thinks it is not really needed 2.97% of the population think its too much painful to test and same number of population think it is too much expensive to test.(Figure-5.19)

Schnipper, Emily E. Barsky showed that glucose management on an academic hospitalist service and the relationship between insulin-ordering practices and glycemic control. The mean rate of hyperglycemia was 31% of measurements per patient. Basal insulin was ordered for 43% of patients, and scheduled rapid- or short-acting insulin was ordered for 4% of patients.

The study showed that 34.65%take oral antibiotic drugs 33.66%take insulin 27.72% take both and 3.96% don't use any medicine to control their diabetes or as a treatment option.(Figure-5.25)

Moreover on the study of treatment and practice of diabetes mellitus it is observed various medicines taken by diabetes patient. It was seen that among them a large population use insulin of about 77%, some patient use metformin hydrochloride of about 69% and small

population use gliclazide, vidagliptin, pramlintide, glibenclamide, tolbutamide, gliclazide, biguanides drugs. Further it was also showed that a large number population don't know about their medicine of about 48 %.(Figure-5.26)

6.2 Conclusion:

People with diabetes may experience many serious, long-term complications. Some of these complications begin within months of the onset of diabetes, although most tend to develop after a few years. Most of the complications gradually worsen. In people with diabetes, strictly controlling the levels of glucose in the blood makes these complications less likely to develop or worsen.

Most complications are the result of problems with blood vessels. Glucose levels that remain high over a long time cause both the small and large blood vessels to narrow. The narrowing reduces blood flow to many parts of the body, leading to problems. There are several causes of blood vessel narrowing. Complex sugar-based substances build up in the walls of small blood vessels, causing them to thicken and leak. Poor control of blood glucose levels also tends to cause the levels of fatty substances in the blood to rise, resulting in atherosclerosis . Levels of glucose in the blood and poor circulation can harm the heart, brain, legs, eyes, kidneys, nerves, and skin, resulting in angina, heart failure, strokes, leg cramps during walking (claudication), poor vision, kidney failure, damage to nerves (neuropathy), and skin breakdown.So control of diabetes is very important and we should be conscious about its harmful consequences.Govt should take necessary steps to control diabetes and grow public awareness.

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