WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 7, Issue 6, 137-148 Research Article ISSN 2278 – 4357

EVALUATION OF STANDARD TREATMENT PROTOCOLS OF DIABETESMELLITUS IN A PRIVATE TEACHING HOSPITAL MIRPUR AJK

Sarwat Shaheen*[1], Anam Sana[1], Habib Ur Rehman[2], Asif Mehmood Hashmi[3], Muhammad Taufiq Ahmad[4] and Nargus Rehman[5]

[1]Mohi Ud Din Islamic Institute of Pharmaceutical Sciences.
[2]Mohtarma Benazir Bhutto Shaheed Medical Collegem Mirpur AJK.
[3]Department of Pharmacy, The University of Poonch Rawalakot AJK.
[4]Akson College of Pharmacy, Mirpur University of Science and Technology, Mirpur AJK.
[5]Department of Eastern Medicine, The University of Poonch Rawalakot AJK.

Article Received on
13 April 2018,
Revised on 04 May 2018,
Accepted on 25 May 2018,
DOI: 10.20959/wjpps20186-11752

***Corresponding Author**
Sarwat Shaheen
Mohi Ud Din Islamic Institute of Pharmaceutical Sciences.

ABSTRACT

Diabetes is a metabolic disorder characterized by elevation of blood glucose by a relative absolute deficiency of insulin. This report is based on clinical pharmacy clerkship conducted during March to August 2014 in Medical ward of MUHAMMADI TEACHING HOSPITAL MirpurAzad Kashmir. The aim of this study was to evaluate the treatment protocols of diabetes. Data of 100patients suffering from NIDDM was collected and following parameters including patient demographics, onset of disease, disease medication history, concurrent diseases and possible complications of diabetes, management plan and treatment outcomes were monitored and compared to standard guidelines. Special area of focus was the standard treatment for the management of DM, and the most frequently used combination of two or more oral antidiabaetic agents, insulin and oral anti diabetic agents.

KEYWORDS: DM: Diabetes mellitus, NIIDM: Non-insulin dependent diabetes mellitus.

INTRODUCTION

Diabetes is a chronic illness which requires the continuing medical care along with patient self-management for the prevention and reduction of acute and long term complications.[1]

The world population is expected to touch the level of 7.9 billion by 2025. 6 countries account for almost 50% of the population increase every year; among these countries, three Asian countries, India, China, and Pakistan, contribute 21%, 12%, and 5%, respectively. Populations of Asia are racially heterogeneous and have differing demographic, cultural, and socioeconomic characteristics. Differences in genetic and environmental attributes which effect diabetogenesis could also be heterogeneous. Type 2 diabetes is studied in Asian countries.[2] It has been observed that type 2 diabetes mellitus progresses along with age and the disease remains controlled up till 5-6 years of diagnosis. The average age of type 2 diabetic patients varies geographically but in majority of the areas onset is between 50 and 60Years.

Diabetes is a chronic illness which requires the continuing medical care along with patient self-management for the prevention and reduction of acute and long term complications.[3] Diabetes is classified into following four clinical classes:

Type 1 diabetes: it results from cell destruction, usually leads to absolute insulin deficiency.

Type 2 diabetes: it results from a progressive defect in insulin secretion on the background of resistance of insulin. Other specific types of diabetes may be due to certain causes e.g.; Genetic defects either in cell function or in insulin action.

Or the diseases of pancreas e.g. cystic fibrosis), or it may be drug induced e.g. in the case of AIDS/HIV treatment or organ transplant.

Gestational diabetes mellitus (GDM): Is diabetes diagnosed during the pregnancy and it is not clearly overt diabetes.

Diabetes mellitus describes a metabolic disorder of multiple etiologies which is characterized by chronic hyperglycemia with disturbances in the metabolism of carbohydrate, fat and protein which result from defects in the secretion of insulin, insulin action or both. The genetic basis of type 2 diabetes mellitus is still unclear, although some promising susceptibility genes have been identified including calpain-10, PPAR-c and Kir 6. which can relate to genetic basis of diabetes type 2. In pancreas islet of Langerhans contains four cell types. These cells synthesize and secrete distinct polypeptide hormones (beta) cells are responsible for insulin synthesis; glucagon is synthesized by A cells, pancreatic polypeptide in PP or F cell. For the maintenance of stable concentrations of glucose in blood both during fasting and feeding, insulin secretion is tightly regulated the regulation of insulin is achieved

by the coordinated interplay of various nutrients, pancreatic hormones, gastrointestinal (GI) hormones and autonomic neurotransmitters. Insulin secretion is stimulated by glucose, amino acids fatty acids and ketone bodies.

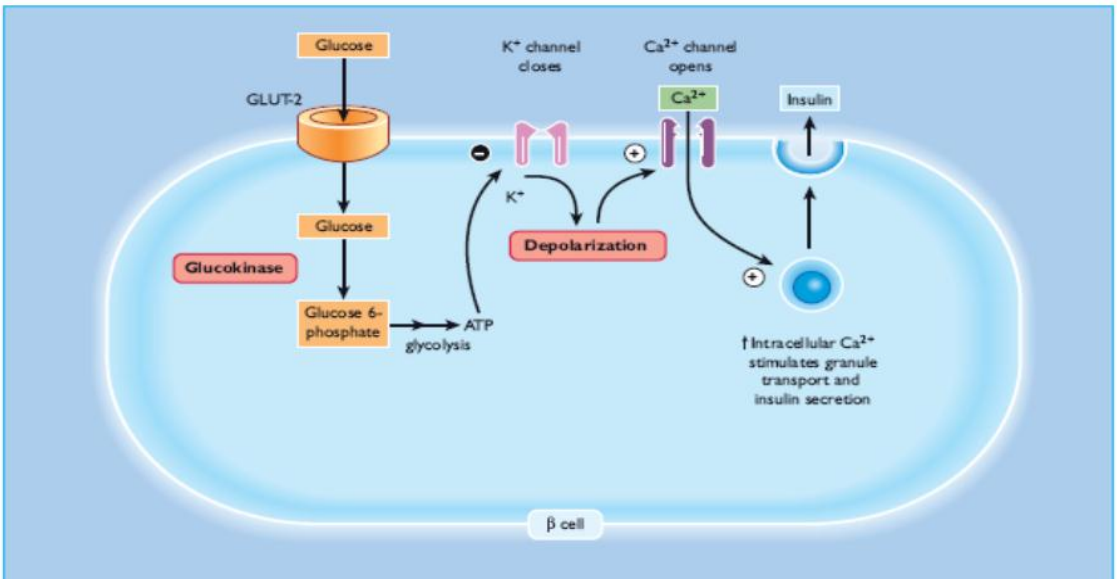

Figure 1: Regulation of Insulin.

Glucokinase is associated with type 2 maturity onset diabetes of the young (MODY), it is a rare monogenic form of diabetes. Due to mutations in this glucokinase its ability to phosphorylated glucose is compromised, threshold for glucose-stimulated insulin is raised and eventually diabetes mellitus results.

Insulin circulates as monomer in blood having volume of distribution approximate to volume of extracellular fluid. In fasting conditions 40 μg (1 unit) of insulin/h is secreted to achieve the concentration of insulin in portal blood to 2–4 ng/mL (50–100 μunits/mL) and its concentration in peripheral circulation is 0.5 ng/mL (12 μunits/mL). after ingestion there is rapid rise in insulin concentration in portal blood, and there is parallel but smaller rise in peripheral circulation. Plasma half life of insulin is 5-6 minutes. Insulinis primarily degraded in liver, kidney and muscles. About 50% of insulin. About 50% of the insulin never reaches the general circulation that reaches the liver via portal vein.Filtration of insulin occurs in renal glomeruli and reabsorbed by the tubules these also degrade it.[4]

***Effects of insulin include*:** Reduction in blood glucose due to increased glucose uptake in the peripheral tissues (which convert it into glycogen or fat), and reduction of hepatic output of glucose. Other metabolic effects. In addition to enabling glucose to pass across cell

membranes, the transit of amino acids and potassium into the cell is enhanced. Insulin regulates carbohydrate utilization and energy production. It enhances protein synthesis. It inhibits lipolysis.[5]

Insulin is the pivotal hormone regulating cellular energy supply and macronutrient balance, directing anabolic processes of the fed state.

Physiologically, at the whole body level, other hormones influence the actions of insulin though insulin is the dominant hormone in driving metabolic processes in the fed state, it acts in concert with growth hormone and IGF-1; among other stimuli growth hormone is secreted in response to insulin, and thus preventing insulin induced hypoglycemia. Glucagon, glucocorticoids and catecholamine are other counter-regulatory hormones, metabolic processes in the fasting state are driven by these hormones. Glucagon enhancesglycogenolysis, gluconeogenesis and also ketogenesis. the degree of phosphorylation ordephosphorylatingof the relevant enzymes is determined by insulin to glucagon ratio. Catecholamine promotes the lipolysis and glycogenolysis; glucocorticoidspromote muscle catabolism, gluconeogenesis and lipolysis. Excess secretion of these hormones may contribute to insulinresistance in particular settings, but does not account for thevast majority of insulin resistant states. In majority of cases Insulin resistance is believed to be manifest at the cellular level via post-receptor defects in insulin signaling. Possible mechanisms include down-regulation, deficiencies or genetic polymorphisms of tyrosine phosphorylation of the insulin receptor, IRS proteins or PIP-3 kinas, or may involve abnormalities of GLUT 4 function.[6]

Diagnosis of diabetes; is done on the basis of plasma glucose criteria, fasting plasma glucose(FPG) or oral glucose tolerance test (2-h value in 75g of oral glucose. In 2009, an international expert committee included representatives of ADA (American diabetes association),the international diabetes federation (IDF), and the European association for study of diabetes (EASD) recommended the use of the A1C for the diagnosis of diabetes with a threshold of 6.5% and this was adopted in 2010 by ADA.the diagnostic test should be performed by the method certified by National Glycohemoglobin Standardization Program (NGSP) and should be standardized to Diabetes Control and Complications Trial(DCCT) reference assay.

A1C _ should be 6.5%. Test should be performed by the method certified in NGSP and DCCT. FPG _126 mg/dl (7.0 mmol/l). For this fasting is defined as no intake of calories for 8hrs. 2-h plasma glucose _200 mg/dl (11.1mmol/l) during oral glucose tolerance test. The test should be performed as the World Health Organization described, by using a glucose load equivalent of 75 g anhydrous glucose dissolved in water. Patient with classic symptoms of hyperglycemic crisis, hyperglycemia a random plasma glucose _200 mg/dl (11.1mmol/l).[7]

Incidence of diabetes varies widely throughout the world. In the U.S., 5–10% of all diabetic patients have type 1 DM, with an incidence of 18/100,000 inhabitants/year. The vast majority of diabetic patients (~90% in the U.S.) have type 2 DM. Incidence rates of type 2 DM increase with age, with a mean rate of about 440/100,000/year by the sixth decade in males in the U.S. Both environmental and genetic components affect the risk of developing DM.[8]

Etiology: Includes different factors for both type 1 and type 2. For type 2 DM Obesity is a major risk factor, and 80–90% of type 2 DM subjects are obese in USA. Studies also support a strong genetic basis for type 2 DM. Mutations in glucokinasecause the autosomal dominant disorder MODY2. Other single-gene mutations cause the other types of MODY, including those affecting pancreatic transcription factors. Type 1 DM involves an autoimmune attack on the pancreatic _ cells and is associated with specific human leukocyte antigen (HLA) alleles, and the HLA complex is known to play critical roles in the immune response. However, the trigger for the immune response remains unknown. In about 10% of new cases of type 1 DM, there is no evidence of autoimmune insulitis. The ADA and the World Health Organization (WHO) therefore subdivide this disease into autoimmune (1A) and idiopathic (1B) subtypes. At diagnosis, virtually all persons with type 2 DM show a profound defect in first-phase insulin secretion in response to an intravenous glucose challenge, although some of _-cell abnormalities may be secondary due to desensitization by chronic hyperglycemia.[9]

Prevalence of diabetes in Pakistan*:* According to WHO, prevalence of diabetes mellitus in Pakistan ranked 8 in the world and with present lifestyle this ratio will increase The prevalence of diabetes in the North West Frontier Province (NWFP) of Pakistan has been reported to be 1.49%. Similarly, the prevalence of diabetes in the Muzaffarabad, Bagh and Poonch districts of Azad Jammu & Kashmir (AJ&K) was 0.95% In district Mirpur, 41 (1.92%) individuals out of 2135 were diabetic. Mirpur city (2.67%) has the higher prevalence than Chaksawari (2.42%) and Dudyal (0.58%) in district Mirpur. Again, male diabetics (1.08%) were more than the females diabetics. (0.84%).[10]

***Standard treatment protocols for diabetes*:** Therapy for type 1 diabetes AccordingtoDCCT intensive insulin therapy (three or more injections per day of insulin, continuous subcutaneous insulin infusion [CSII], or insulin pump therapy) was a key part of improved glycemia control and better outcomes. Therefore, recommended therapy for type 1 diabetes includes the following components: 1) use of multiple-dose insulin injections (three to four injections per day of basal and prandial insulin) or CSII therapy; 2) matching prandial insulin to carbohydrate intake, premealblood glucose, and anticipated activity; and 3) for patients in which especially if hypoglycemia is a problem), use insulin analogs.

Medications: Management of diabetes include insulin and other oral antidiabaetic agents
Insulin is of following types.

1. *Short duration of action (and rapid onset*): Soluble Insulin (neutral insulin). Recent advancement to this class is, insulin lispro (Humalog), it is a modified human insulin in which there is reversing of two amino acids thus it resulted in a very rapid onset of action (within 15 minutes of injection). Insulin aspart is similar.

2. *Intermediate duration* of action (and slower onset): Isophane Insulin, a suspension with protamine; Insulin Zinc Suspensions, amorphous or a mixture of amorphous and crystalline

3. *Longer duration* of action: Insulin Zinc Suspension, crystalline, or Protamine Zinc Insulin (insulin in suspension with both zinc and protamine).

4. A*mixture* of soluble and Isophaneinsulins, officially called *biphasic* insulins. The short acting analogue insulins are now also available in mixtures. Other mixtures are also available, but are not used frequently.

Soluble insulin inj. (neutral, regular insulin) is an aqueous solution of insulin It is simple to use, isgivens.c. 2-3 times a day, 30 min before meal times. If it is used sensibly it shows little hypoglycemic reactions. The insulin injection should be delayed if the meal is delayed. The dose can easily be adjusted according to self-performed blood glucose measurements.

Intravenous soluble (neutral) insulin is used in diabetic ketoacidosis DKA. It may be given intermittently (i.v. or i.m.) but continuous infusion ismorepreferred.

Initial treatment for a Type 1* (IDDM) *patient, who does not present diabetes ketoacidosis, will usually be outside hospital with two injections of intermediate acting insulin, or mixed insulin. Other permutations can be followed later, including soluble insulin before each meal, and intermediate-acting insulin at bedtime. The following is a guide to initial daily dose requirements: 0.3 units/kg (16-20 units daily).

According to the usual monitoring of blood glucose dose is adjusted). Daily (total) dose increments should be 4 units at 3-4-day intervals. If it is decided to give the patient only one injection per day, then 10-14 units of an intermediate-acting Isophane suspension may be given. Dose increments (4 units) may be made on alternate days. According to patient response soluble insulin (neutral) may be added, or mixed (biphasic) insulins may be used,. *When stable,* patients usually receive either biphasic insulin or a mixture of soluble, short-acting human insulin, and a longer-acting suspension of insulin with protamine or zinc. Excessive doses of insulin leads to obesity and over eating; it can also cause hypoglycemia (especially nocturnal), that may be followed by rebound hyperglycemia in morning that is mistakenly treated by increased insulin, thus establishing a vicious cycle Somogyi effect.[11]

ORAL ANTIDIABETIC AGENTS

Table 1: Oral antidiabaetic agents.

Class	***Use***	***Contraindication***	***MOA***	***Adverse effect***	***Interactions***
1.Bigunaides					
*metformin	Ist choice for obese type2 pt	Renal failure, alcoholics, lung & cardiac disease and acute MI	Reduced glucose absorption from gut, inhibition of gluconeogensis	Nausea,anor-exia, vomiting Metallic taste	Other agents are additive, ethanol causes metformin induced lactic acidosis
2.sulfonylureas					
*tolbutamide *glibenclamide *glicalizide	For type 2 pts who have not responded with metformin or diet		. Sulphonylurea, like depolarize B cells and release insulin by binding to sulphonylurea receptors (SUR) and blocking ATP-dependent potassium channels (KATP);activates voltage-sensitive Ca2_ channels, in turn causing entry of Ca2_ ions and insulin secretion.	Hypoglycemia Allergic reactions, fever Rashes, GI upset	MAOI potentiates activity Growth hormones and glucocorti-Coides antagonize.
Thiazolidinediones (Glitazones)					
*pioglitazone *rosiglitazone	Glitazones lower blood glucose &hemoglobin A1c in type 2 diabetes mellitus patients who are inadequately controlled on diet alone or diet and other oral drugs.	Hepatic impairment, liver disease Heart failure	Bind to peroxisome proliferating Activator receptor found in hepatocytes and adipocytes	Weight gain, Fluid retention	Additive with oral agents, Potentiate Insulin
Acarbose	Type 2 diabetics inadequately treated with other agents		Acarboseis a reversible competitive inhibitor of intestinal α-glucoside hydrolases and delay the absorption of starch and sucrose,	Flatulence, Abdominal Distention diarrhea	

METHODOLOGY

It was observational type of study designed to determine rationality of prescribing practices in patients of different age groups suffering from diabetes. This study was designed on IN and OUT patients in Mohammadi teaching hospital Mirpur Azad Kashmir. Different parameters were observed during the study including Age, weight, Gender concurrent disease current blood glucose level, drug interactions and drug related problems. We collected data on data sheets mentioned in the later sections and applied statistics using Ms Excel.

RESULTS AND CONCLUSION

Table 2. Gender wise distribution of disease.

Gender	Total patients
Male	46(46%)
Female	54 (54%)

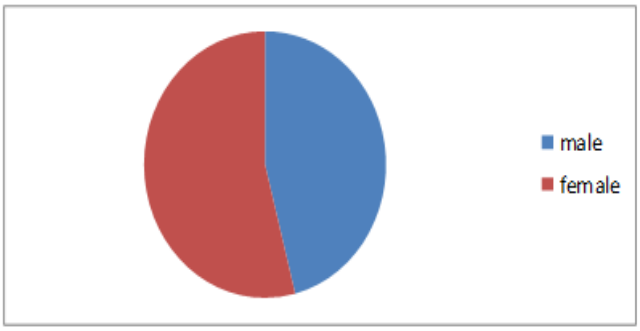

Figure 1: Gender wise distribution of diabetes.

Table 3: Types of diabetes.

Type	No. Of patients	Male	Female
Type 1	2(4%)	0	4(4%)
Type2	97(97%)	46(46%)	48(48%)
Gestational diabetes	1(2%)	0	1(2%)

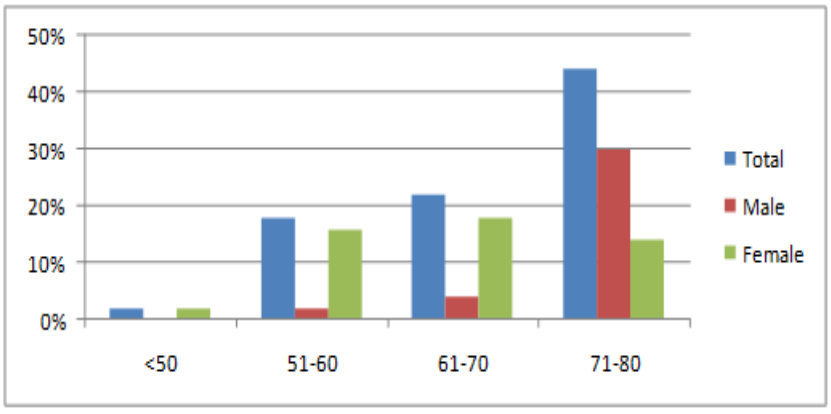

Figure 3: Prevalence of different types of different types of diabetes in both genders.

Table 4: Weight wise distribution.

Weight (kg)	Total patients	Male	Female
<50	1(1%)	0	1(1%)
51-60	18(18%)	02(2%)	16(16%)
61-70	22(22%)	4 (4%)	18(18%)
71-80	44(44%)	30(30%)	14(14%)
>80	14(14%)	10(10%)	4 (4%)

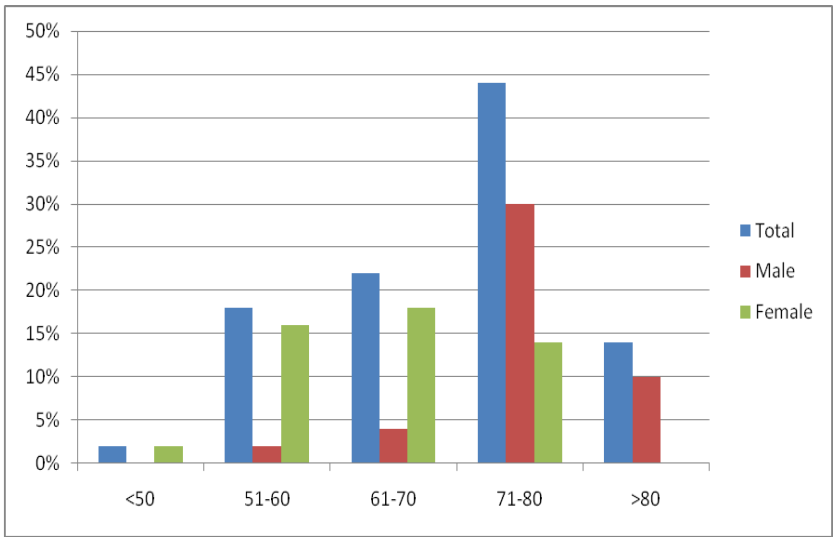

Figure 4: Prevalence of diabetes in different weight categories.

Table 5: Age wise distribution of disease.

Age (yrs)	Total patients	Male	Female
<20	1(1%)	0	1(1%)
20-40	18(18%)	2(2%)	16(16%)
40-51	44(44%)	30(30%)	14(14%)
51-60	22(22%)	4(4%)	18(18%)
60-80	14(14%)	10(10%)	4(4%)

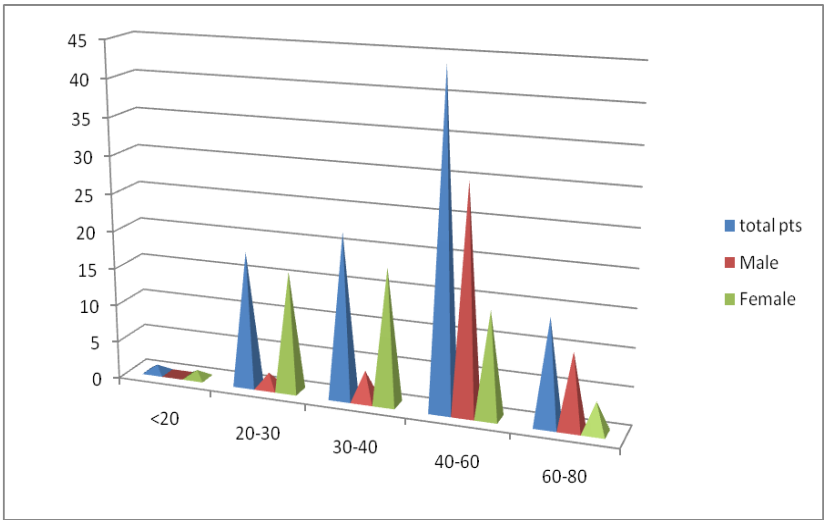

Fig 5: Weight wise distribution of diabetes.

5. Family History

16(16%) out of 100 patients had family history of diabetes. Other most prevalent diseases were hypertension and hyperlipidemia.

25 (25%) out of 100 patients had hypertension and were taking medications for it. 36(36%) out of 100 patients were being treated for hyperlipidemia.

6. Diabetic complications

6(6%) out of 100 patients had diabetic complications i.e peripheral neuropathy and diabetic retinopathy. Diabetic foot ulcer.

7. Patient's medical history

58 out of 100 patients had no history of any major illness where as 42(42%) patients were already suffering from some kind of illness and were using medications for their treatment.

Patient drug therapy

Patients on monotherapy with insulin

Total 28patients were on insulin therapy

Total 6 patients were on insulin and single oral antidiabaetic agent

44 patients were on monotherapy with oral antidiabaetic.

22 patients were on more than one oral antidiabaetic agents.

Table 6: Drug therapy.

Drug therapy	No. of prescription	%age of prescription
Insulin therapy	28	28%
Single oral antidiabaetic	44	44%
Insulin +oral antidiabaetic	6	6%
Multiple oral antidiabaetic	22	22%

Table 7: Pattern use of various classes of antidiabaeticagents.

Antidiabetic class	Overall prescription frequency	Monotherapy prescription frequency
Insulin	32 (32%)	8(8%)
Sulphonylurea	40(40%)	18(18%)
Biguanides	18(18%)	6(6%)
Pioglitazone	16(16%)	

REFERENCE

1. American Diabetes Association.Standards of Medical Care in Diabetes—2011. Diabetes Care, 2011; 34(1): S11-S61. doi:10.2337/dc11-S011.
2. Ramachandran, A., R. C. Wan Ma, et al. "Diabetes in Asia." The Lancet, 2010; 375(9712): 408-418.
3. American Diabetes Association. Standards of Medical Care in Diabetes—2011.Diabetes Care, 2011; 34(1): S11-S61. doi:10.2337/dc11-S011.
4. GOODMANGILLMAN(2008).<Goodman_Gillman_Manual_of_Pharmacology_therapeutics_2008.pdf>.
5. Lawrence, b. <Bennet Lawrence - Clinical Pharmacology.pdf>.
6. Gisela Wilcox, Clin Biochem Rev Vol 26 May 2005.”Insulin and insulin resistance.
7. American Diabeted Association."Standards of medical care in diabetes—2011." Diabetes care, 34: S11.
8. GOODMANGILLMAN(2008).<Goodman_Gillman_Manual_of_Pharmacology_therapeutics_2008.pdf>
9. GOODMANGILLMAN(2008).<Goodman_Gillman_Manual_of_Pharmacology_therapeutics_2008.pdf>
10. Khan, S., M. Abbas, et al. "Prevalence of diabetes mellitus in Mirpur and Kotli districts of Azad Jammu & Kashmir (AJ&K)." SARHAD JOURNAL OF AGRICULTURE, 2007; 23(4): 1141.
11. Therapeutics, T. o. c. p. a. <A Textbook of Clinical Pharmacology and Therapeutics.pdf>.