

Rational Drug Therapy for the Management of Diabetes Mellitus

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ABSTRACT

Diabetes Mellitus is one of the major worldwide public health issues, along with socio-economic growth. Diabetes Mellitus is a chronic metabolic syndrome of several causes characterized by long-lasting hyperglycemia with the turmoil of carbohydrates. The study aimed to evaluate pharmacotherapy on rational grounds for drug-drug interactions, polypharmacy, and untreated conditions if any. For the recording of patient case histories, a standard questionnaire was designed, which includes age, sex, history, chief complaints, Clinical tests, diagnosis & patient's family history, etc., the copy of which is appended. Considering 20 cases, different parameters were studied which showed that 17 out of 20 cases received rational therapy according to standard pharmacotherapy and the patients responded well to the prescribed therapy, 3 cases out of 20 received irrational therapy due to which they showed poor response. The percentage of the female patient was 40% and the male patient was 60%. In some of these cases, drug interactions were found and their percentage was 22.1%. The most prominent interaction occurrence was of Ramipril with metformin i.e. 18.75% and Ciprofloxacin interaction with glimepiride is 6.25% etc. In all cases, a total of 86 drugs related problems were reported. The percentage of untreated conditions was 9.3%, drug without indication 6.98%, and cost-related problems were 20.9%, etc. In some cases, concurrent diseases were also found i.e. hypertension at 37.5% and asthma at 25 was prominent. Patients with ages between 41-50 and 51-60 years have a high percentage of Diabetes Mellitus i.e. 40% and 40% respectively. The most prominent ADRs were insomnia, skin rashes, dizziness, nausea, vomiting, diarrhea, etc. Nausea, vomiting, and diarrhea are more frequent with antibiotics.

Keywords: Epidemiology, Etiology, Pathophysiology, Investigations, Complications and Treatment of Diabetes Mellitus

INTRODUCTION

Diabetes Mellitus is one of the major worldwide public health problems, along with socio-economic growth¹. Diabetes Mellitus is a chronic metabolic syndrome of several causes characterized by long-lasting hyperglycemia with the turmoil of carbohydrates, protein, and lipid metabolism resultant from some failure in insulin secretion, insulin action, or both². The consequence of diabetes mellitus encompasses long-lasting damage, disordering, and letdown of a range of organs. Diabetes mellitus is characterized by rough signs like excessive thirst, polyuria, weight loss, and blurring of vision³. The most severe forms are ketoacidosis (high level of ketones in the blood) and a non-ketonic hyperosmolar state may develop leading to coma, and if untreated may even cause death⁴. The causes of diabetes mellitus are quite moderately identified. The research shows that there are various causes involved that cause diabetes. But the main reasons involved in diabetes mellitus are genetic factors and environmental factors⁵.

Diabetes mellitus is a more heterogeneous syndrome than the simple subdivision into type 1 diabetes and the second one is type 2 diabetes⁶. A better classification of diabetes mellitus is based on variances in pathophysiology, factors, and prognosis⁷.

Type 1 diabetes mellitus is triggered by the destruction of the beta cells of the pancreas. The inherently susceptible individuals are more predisposed to this progression and are produced by an environmental factor⁸. Type 2 diabetes mellitus, is also well-known as non-insulin-dependent. Diabetes mellitus (NIDDM), is the distant further common assortment 80–90 % and is partial to adults⁹. Ecological aspects particularly certain viruses are involved in the production of diabetes type 1. Some extra environmental elements that may produce the auto-immune devastation of beta cell of the pancreas Such as certain chemicals, dietary factors in initial life (Vitamin D deficiency, Exposure to cow's milk), cytotoxins, Enteroviruses, and some other infections^{10,11}.

The American Diabetes Association (ADA) states that Diabetes type 2 has a more resilient link to family history and line than type 1 diabetes. While genetics plays a vital part in the development of type 2 diabetes¹². The bigger parts (around 97 %) of diabetic patients have type 2 diabetes. The frequency of this type 2 diabetes is speeding progressively. Several genes are intricate in developing diabetes type 2 such as the Gc genotype gene located

on chromosome 4, the HLA gene on the chromosome, the Lipoprotein antigen gene on chromosome 6, and many others¹¹. Obesity is one of the most important factors for the development of type 2 diabetes. Numerous other factors also play a very important role in the development of type 2 diabetes such as age presence of the metabolic, and a sedentary lifestyle¹³. Third most important diabetes is Gestational diabetes which happens during pregnancy and can cause some hitches throughout gestation and at birth and upsurges the risk of type two diabetes in the mother and obesity in the children¹⁴.

Diabetes is extensively recognized as an emerging epidemic that has an increasing impact on almost every nation, and age group worldwide¹⁵. IDF and WHO 2019 to frequently update reports regarding diabetes. In the year 1994, 110 million public globally were valued to have diabetes, and in 2010 the quantity was predicted to upsurge to 239 million people and predicted that 300 million would have diabetes by 2025. An advanced report advised that 171 million persons had diseases in 2000, which would upsurge to 366 million through 2030^{16,17}.

On World Diabetes Day In November 2021, the International Diabetes Federation (IDF) released a new report viewing that 537 million adults are affected by diabetes globally. IDF estimations from the year 2017 show that more than 96,000 new cases of type one diabetes are diagnosed worldwide per year in adolescents and children aged¹⁸. According to the IDF, in Pakistan 1 in 4 adults (26.7%) breathe with diabetes, and has the uppermost diabetes prevalence worldwide¹⁹. The nations with the highest ten highest burdens of diabetes are the USA, India, Brazil, China, the UK, the Russian Federation, Algeria, Saudi Arabia, Nigeria, and Germany. The prevalence of diabetes in Europe and North America has an intermediate incidence or high, the prevalence in Africa is mostly intermediate, and that in Asian countries generally is low, with the remarkable exception of Kuwait¹⁸.

The diagnostic standard for the analysis of diabetes mellitus has been undergoing review internationally. The American Diabetes Association (ADA) and WHO have continuously released differing endorsements regarding the criteria for the identification of diabetes mellitus. In 2003 the ADA changed its references after differences between its recommendations and with WHO³.

The mainstream of diabetes cases is type 2 is preventable to a great range. Regrettably, the etiology of type 1 diabetes is

unidentified, and it remains unavoidable. Quite a few approaches have been and are being strained, up to now with little achievement¹⁴.

METHODOLOGY

This report is based on clinical pharmacy clerkship rotations completed during the training period of 3 months in the endocrinology ward of Lady Reading Hospital Peshawar, KPK, and Pakistan.

Patients with **Diabetes Mellitus** (n =20), admitted to the hospital during the said period were included in this work. Following data was collected:

- Patient's demographic information,
- Chief complaints
- History of current illness
- Past medical history
- Past surgical history
- Family history
- Personal history
- Social history
- Allergies
- Medication history
- Review of systems
- Positive findings of physical examination
- Other relevant histories
- Laboratory data
- Diagnosis
- Drug therapy provided in the hospital
- Monitoring notes
- Discharge medications
- Treatment outcomes
- Other patient information

Data analysis

- The medication history of each patient was analyzed for drug allergies, response, undesirable effects, compliance, and its applications in the assessment and management of the patient's current medical problems.
- Current therapy provided in the hospital was analyzed for its indications and outcomes.
- The whole medication therapy provided in the hospital was analyzed for drug-related problems and their management.
- Any drug information /therapeutic –consultation or patient education and counseling that were provided during rotations were also reported.

RESULTS

This study was conducted in the endocrinology ward of Lady Reading hospital Peshawar. During the study period, prescriptions of 20 patients were collected and thoroughly analyzed. The study group was heterogeneous including both clinical and surgical patients with diverse reasons for their hospitalization. In this whole period of 3 months, 29 different drugs were prescribed. We are here in Lady Reading Teaching Hospital Peshawar for the clerkship of 3 months in which I remain in the Endocrinology Ward. In this current study n= 20 patients, 45 % of patients belongs to Peshawar, 10 % of patients were found in each Mohmand agency, 10 %, Dir 10 %, 10 % Parachinar, Kohat 5 % Charsadda 5 %, Bajaur 5 % Swabi, and 5 % infected individuals belong to Chitral (Table 1).

Table 1: Geographical Distribution of Patients

Place/Address	Frequency	Percentage%
Peshawar	09	45%
Mohmand agency	02	10%
Dir	02	10%
Parachinar	02	10%
Kohat	01	5%
Charsadda	01	5%
Bajaur	01	5%
Swabi	01	5%

Chitral	01	5%
Total	20	100%

In 20 case histories on "Diabetes Mellitus," there were 50 percent males and 50 percent females (Table 2).

Table 2: Gender Wise Distribution of Patients

Gender	Frequency	Percentage%
Male	10	50%
Female	10	50%
Total	20	100%

In this study, the highest number of 45 % of diabetes hospitalized patients were found in the age group 51-60 years and the highest number of 20 % of hospitalized patients were found in the 10-20 years age group, 15 % in 41-50, and 61-70, years age group, while no any hospitalized patient was found in 31-40 (Table 3).

Table 3: Distribution of patient's age wise

Age of patients	Number of patients	Percentages
10-20 Years	4	20%
21-30 Years	1	5%
31-40 Years	0	0%
41-50 years	3	15%
51-60 years	9	45%
61-70 years	3	15%

All these histories to find out the irrationality, adverse drug reactions (ADRs), pharmaco-economic consideration, and noncompliance issues but I did not find these drug-related problems in the "Endocrinology Ward" unfortunately there were many drug-drug interactions in these histories (Table 4).

Table 4: Distribution of patients based on causes of hospitalization

Causes	Number of patients	Percentages
Weight loss	8	40%
Polyuria	4	20%
Diabetic foot ulcer	3	15%
Heart problem	2	10%
Vision deterioration	3	15%

The greatest percentage of drug interactions was found between "insulin & aspirin", which was 40 percent of all case histories. The second highest percentage was found between Metformin & Insulin and Duloxetine & Aspirin which was 15 percent. The percentage of interaction between Amoxicillin & Aspirin was 10 percent. In all other drug interactions, the percentage accounted for about 5%. The main reason for such drug interaction was poly-pharmacy because in diabetes we know that there are a lot of complications that occur along with diabetes, So many drugs were prescribed there for the management of all these complications, especially in the patient with Type 2 Diabetes Mellitus. We also know that in multiple therapies the chances of drug interactions are always more. Here in LRH one main cause of these drug interactions was the lack of communication between the Physicians and the health care professionals. So there is a need for a proper communication system to exist which can help to overcome all these problems. And this can be done by appointing a Clinical Pharmacist in the "Endocrinology Ward" as well as in the hospital who may minimize this gap by educating the health care professionals and even the patients too by proper counseling about their therapy regime and physical activity.

Table 5: Various drug interactions

Name of drug	Number of interactions	Percentages
Aspirin+Bisoprolol	1	5%
Metformin+Insulin	3	15%
Aspirin+Insulin	8	40%
Duloxetine+Aspirin	3	15%
Piperacillin+Aspirin	2	10%

Enoxaparin+Aspirin	2	10%
Aspirin+Atenolol	1	5%
Dimenhydrinate+prochlorperazine	1	5%
Duloxetine+Tramadol	1	5%
Piperacilline+Enoxaparin	1	5%
Mefenamic acid+Ramipril	1	5%
Ramipril+Aspirin	1	5%
Ramipril+Insulin	1	5%
Amoxicilline+Aspirin	2	10%
Candesartan+Nebivolol	1	5%
Candesartan+Insuline	1	5%
Candesartan+Aspirin	1	5%

Table 6: Significant findings of Medication History

Finding of Medication History	Frequency
No Of Cases Taken	20
No Of Past Medication History Recorded	04
Average No of Drugs Used	09
Compliance	15
Non-Compliance	05
Positive Response to Therapy	16
Improper Response to Therapy	04

Table 7: Brands Statistic in Past Medication History

Drug Brands	Frequency
Ramipace	03
Glucophage	03
Panadol	08
Loprin	04
Gravinate	05
Lasix	09
Zodip	11

Table 8: Dosage Forms Based Statistic in Past Medication History

Dosage Form	Frequency	Percentage
Injection	66	40.9%
infusion	07	4.3%
tablet	75	46.5%
syrup	06	3.7%
nebulizer	04	2.4%
capsule	03	1.8%
total	161	100%

Table 9: Drug Generic Based Statistic in the Treatment of DM

Generic	Frequency
Insulin preparations	18
Aspirin	10
Sulbactam+cefoperazone	9
Rosuvastatin	7
Paracetamol	4
Metronidazole	4
Clindamycin	4
Atorvastatin	4
Co-amoxiclav	4
Metformin	3
Duloxetine	3
Pregabalin	3
Enoxaparin	3
Ceftriaxone	2
Piperacillin+tazobactam	2
Tramadol	2
Bisoprolol	1
Atenolol	1
Meropenem	1
Dimenhydrinate	1
Sodium picosulfate	1
Prochlorperazine	1
Ramipril	1
Nebivolol	1
Candesartan	1
Citalopram	1
Multivitamin	1
Losartan potassium	1
Alprazolam	1

DISCUSSION

In 20 case histories on "Diabetes Mellitus" there were 50 percent males and 50 percents females. The greatest percentage of drug interactions was found between "insulin & aspirin", which was 40 percent of all case histories. The second highest percentage was found between Metformin & Insulin and Duloxetine & Aspirin which was 15 percent. The percentage of interaction between Amoxicillin & Aspirin was 10 percent. In all other drug interaction the percentage was accounted about 5%.

Approximately, 26.9% of adults living with diabetes in Pakistan are undiagnosed¹⁹. Diagnosis timely and treatment are important in patients with diabetes mellitus. Several of the worries linked with diabetes, for example, retinopathy, cardiovascular disease, nephropathy, neuropathy, stroke, and death, can be behind or prevented with proper treatment of raised blood pressure, and blood. glucose, and lipids²⁰.

A blood level of 200 mg/dL or more strongly directs diabetes. Postprandial blood Glucose is a very important test to diagnose diabetes mellitus²². Oral Glucose Tolerance Test (OGTT), postprandial blood Glucose, and Glycated Hemoglobin the amount of HbA1c made is directly proportional to the typical plasma glucose concentration that the red blood cells are wide-open to through their 120-day life span²². Numerous latest pharmacological agents have been developed to enhance the control of type 2 diabetes mellitus²³. Insulin was the foremost treatment for diabetes. Weight gain can occur after therapy initiation and is typically about 2 to 4 kg. A maximum of the brands of insulin are available in both vial and pen form for delivery. Better glycemic control and improved management of other identified risk factors for the worries of diabetes^{2,24}.

In Pakistan and especially in KPK the prevalence and hospitalization of diabetes patients data are limited. A study documenting the prevalence of diabetes reported that the highest number of diabetes patients were found in Sindh province and the lowest in Khyber Pakhtunkhwa (KPK)²⁵. Similarly, the Frequency of diabetes in urban is also high as compared to the ruler areas was 28.3 % and 25.3 %, respectively²⁶. Our results indicated that the prevalence and hospitalization rate of diabetes patients are higher in urban areas due to obesity, hypertension, sedentary lifestyle, etc., and these results are supported by a study conducted on glucose intolerance and associated factors in Punjab Pakistan²⁷.

This study's finding was very similar regarding different age groups of hospitalization as compared to a study conducted by Shah et al 2020 the 51-60 20 % and 71-80 22.5 % years age group²⁸.

The main reason for such drug interaction was poly-pharmacy because in diabetes we know that there are a lot of complications occur along with diabetes. So many drugs were prescribed there for the management of all these complications especially in patient with Type 2 Diabetes Mellitus. We also know that in multiple therapies the chances of drug interactions are always more. Here in LRH one main cause of these drug interactions was the lack of communication between the Physicians and the health care professionals. So there is a need of proper communication system to exist which can help to overcome all these problems. And this can be done by appointing clinical Pharmacist in the "Endocrinology Ward" as well as in the hospital who may minimize this gap by educating the health care professionals and even the patients too by proper counseling about their therapy regime and physical activity.

CONCLUSION

The majority therapies of for diabetes mellitus were according to the need of patients and covered all aspects of the disease. There were no ADRs, overdose, wrong selection, drugs without indication, duplication, and wrong dosage form found but due to polypharmacy and complex pathophysiology of diabetes, there were a lot of interactions between the drugs were determined which can be managed with proper time adjustment and meaningful communication between health care providers. Pharmacists are

present there in our ward but mostly work as diabetic educators and they do not interact directly with drugs. At the end of my clerkship finally, I concluded that a proper dose calculation system should be introduced, the pharmacoeconomic study should be included practically in hospitals, a proper communication system should be developed, and pharmacists should be hired inwards to take care of medication directly and new health care centers should be established to reduce the burden on present centers otherwise attaining rationality will be difficult to achieve.

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