

Analysis of Adverse Drug Reactions in Patients with Diabetes Mellitus at Private clinics in Hyderabad, Pakistan

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ABSTRACT

Background: Diabetes is characterized by hyperglycemia, a metabolic disorder resulting from defects in insulin secretion, action, or both. The traditional treatment choices available for diabetes include medications that are oral hypoglycemic agents and insulin. Due to the introduction of several medications during the past 20 years, the identification of adverse drug reactions has gained importance.

Aim: The aim of this study was to evaluate the adverse drug reactions among diabetic patients and patients' variables that were linked to the adverse drug reactions.

Study Design: Cross-sectional study

Place and Duration of Study: This research was done at private clinics in Hyderabad, Pakistan, from August 2021 to January 2022.

Methodology: Three hundred and seventy seven participants and the data regarding baseline characteristics of participants, adverse drug reactions reported were analyzed together with the assessment of causality and severity of unwanted reactions.

Results: Two hundred and forty one (63.9%) were males and 136 (36.1%) were females. Only 19 (5%) reported adverse drugs reactions. Hypoglycemia was the most commonly reported adverse drug reaction i.e.11 ((57.9%). On causality assessment, most of the adverse drug reactions fell under the category of probable adverse drug reaction i.e.15 (78.9%). Four (21.1%) of them had the doubtful relation with the medications. The majority of the adverse drug reactions that were reported by the participants were found to be moderately severe 13 (68.4%), when analyzed through severity assessment scale. Six (31.6%) were belonged to mildly severe category.

Conclusion: The upper age group, male gender, and diabetes duration of more than 5 years were associated with a higher incidence of adverse drug reactions. This study gave in depth analysis of adverse drugs reactions reported in the patients of diabetes mellitus together with the nature of adverse drug reactions reported. A better patient outcome would result from the clinical pharmacist's active participation in adverse drug resistance.

Keywords: Adverse drug resistance (ADR), Diabetes mellitus, Hypoglycemia, Severity

INTRODUCTION

Diabetes is characterized by hyperglycemia, a metabolic disorder resulting from defects in insulin secretion, action, or both. Diabetes' chronic nature is linked to long-term harm, malfunction, and failure of many organs, including the heart, blood vessels, kidneys, nerves, eyes, and kidneys.¹ Diabetes managerial strategies put a strong emphasis on preventing illness, evaluating high-risk populations, and aggressively treating people who are pre-diabetic. For the majority of these individuals, medicinal therapy continues to be the primary option.² The traditional treatment choices available for diabetes include medications that have been on the market for a while. They are the most often utilized medical intervention to alleviate pain, however drugs can be lethal and can cause unwanted serious drug reactions that can range from moderate to catastrophic. Despite their effectiveness in establishing glycemic control, anti-diabetic medications have various safety concerns.^{3,4}

According to the World Health Organization (WHO), adverse drug responses are any reaction to a medicine that is harmful and unanticipated that takes place at dosages typically used in humans for disease prevention, diagnosis, or treatment, or to alter physiologic function. This definition thus does not include drug addiction, deliberate or unintentional overdosing, therapeutic failure, or medication mistakes.⁵⁻⁷

Due to the introduction of several medications during the past 20 years, the identification of adverse drug reactions has gained importance. Adverse medication responses can happen often in hospitals, negatively compromising patient care and frequently leading to high rates of morbidity and mortality. The market's expanding medication supply and a rise in polypharmacy are two variables that have contributed to ADRs' rising occurrence globally. Adverse drug responses can cause patients to lose trust in their doctors' ability to treat them, which can lead to unfavourable feelings about it. Patients may also choose to self-treat, which might lead to more ADRs.^{8,9} ADRs pose a serious threat to public health in regard to mortality, morbidity, and financial burden.¹⁰

"The science and actions connected to the identification, evaluation, comprehension, and control of ADRs or other drug-related issues," according to the WHO, are what are meant by pharmacovigilance. It can assist in continuously delivering information on the integrity of drugs being used.^{11,12}

The rising use of anti-diabetic drugs emphasizes the necessity for clinical pharmacists to monitor patients and report any suspected ADRs to identify and evaluate the ADRs in diabetes mellitus patients, including a causation and severity evaluation.

MATERIALS AND METHODS

This cross-sectional study was carried out in patients with diabetes mellitus who visited private clinics of Hyderabad, Pakistan and satisfied the inclusion criteria. To establish a 95% confidence interval (CI) with a 5% margin of error, a total sample of 377 was enrolled. Rao Soft's online sample size calculator was used to determine sample size. Utilizing a simple random sample approach, participants were chosen. The medication adverse reactions probability scale (Naranjo) as well as the hart wig and Siegel scale, respectively, were used to further evaluate the causation and severity of the participants' reported adverse drug responses. Before entering the information into the form, it was all double verified for accuracy. SPSS-16 was used to analyze the collected data.

RESULTS

The majority of the patients, 131 (48%) were between the ages of 41-50 years and 148 (39.3%) between 51-60 years. Two hundred and nine (55.4%) had diabetes for longer than 5 years. There were 241 (63.9%) males and 136 (36.1%) females (Table 1). There were 19 (5%) individuals having an ADR (Fig. 1). The ADR that was most frequently reported was hypoglycaemia 11 (57.9%) followed by memory loss 4 (21.1%), weight gain 2 (10.5%), UTI 1 (5.3%), and pancreatitis 1 (5.3%) [Table 2]. ADR and anti-diabetic medication interactions were assessed using the adverse drug reaction probability scale (Naranjo). Fifteen (78.9%) of the adverse drug events had a likely relationship with the medicines, whereas 4

(21.1%) had a dubious relationship (Fig. 2). Using a modified Hart-Wig-Siegel scale, the severity of the ADR was evaluated. ADRs were reported to be mild in 6 (31.6%) and moderate in 13 (68.4%) of the cases (Fig. 3). The co-relation of ADRs with the age ($p=0.000$), gender ($p=0.675$) and duration of diabetes ($p=0.034$) of the patients was evaluated. Males ($n=13$) were found to have a higher incidence of ADRs than females ($n=6$). The majority of ADRs ($n=14$) were detected in the older age group. Participants with diabetes for more than five years reported the majority of ADRs ($n=15$) [Table 3].

Table 1: Baseline characteristics of participants

Characteristics	No.	%
Age (years)		
30-40	2	0.5
41-50	181	48.0
51-60	148	39.3
>60	46	12.2
Gender		
Male	241	63.9
Female	136	36.1
Duration of diabetes (years)		
< 5	168	44.6
>5	209	55.4

Table 2: Classification of reactions from the reported ADRs

Adverse drug reactions	No.	%
Memory loss	4	21.1
Weight gain	2	10.5
Hypoglycemia	11	57.9
UTI	1	5.3
Pancreatitis*	1	5.3
Total	19	100.0

*Radiological evidence of gallstones was present

Table 3: Association of ADRs with Baseline Characteristics (n=19)

Characteristics	ADRs	P value
Age (years)		
30-40	1	0.000
41-50	1	
51-60	3	
>60	14	
Gender		
Male	13	0.675
Female	6	
Duration of diabetes (years)		
< 5	4	0.034
>5	15	



Fig. 1: Incidence of ADRs

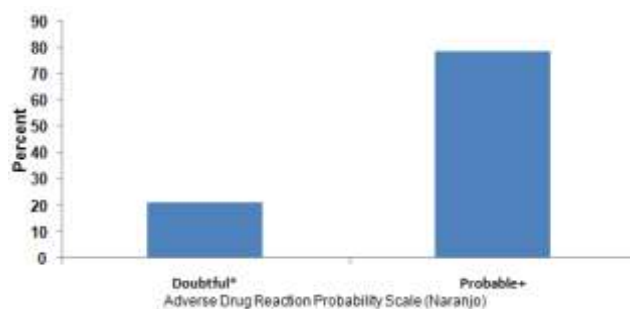


Fig. 2: Evaluation of ADRs based on causality

+Probable ADRs include pancreatitis, UTI, weight gain & hypoglycaemia
*Doubtful ADRs include memory loss

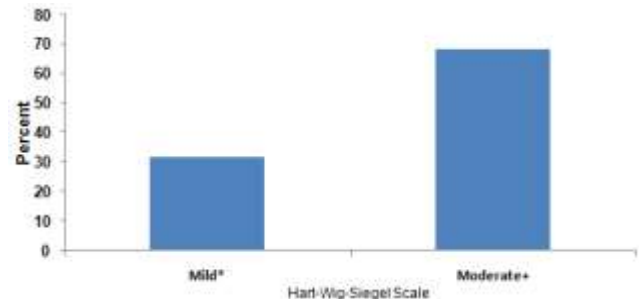


Fig. 3: Evaluation of severity of ADRs

+Pancreatitis, UTI, hypoglycaemia were moderate in severity
*Memory loss and weight gain were mildly severe ADRs

DISCUSSION

Adverse drug reactions to medications do occur often, however they are frequently underreported. Anti-diabetic medicines help people with diabetes mellitus better regulate their blood glucose levels. However, unfavourable side effects from medications have often been linked to non-compliance, which results in therapeutic failure, additionally, a longer hospital stay and higher medical expenses.¹³ Drugs used to treat diabetes are not an exception. Early detection of these ADRs and knowledge of their type and severity enable effective therapy.

Adverse drug reactions severity was assessed using a modified Hart-Wig-Siegel scale, and the majority of ADRs reported in the research were moderate in severity 13 (68.4%), proceeded by mild ADRs 6 (38.6%). According to the Hart-Wig and Siegel severity assessment scale, which was used in the study by Keezhipadathil¹⁴, the majority of the ADRs reported in the study, 30 were moderate in character, followed by 28 ADRs that were mild in severity. The Naranjo scale was used in the study by Keezhipadathil¹⁴ to evaluate the ADRs, and it revealed that the most of the adverse drug events, 53 were probable, which is consistent with the results of the current study.

Hypoglycemia was the most prevalent ADRs 11 (57.9%). Skipping meals, over-prescribing combination medication in individuals who could have controlled their glycemic control with monotherapy and lifestyle changes and over-prescribing insulin with secretagogues were the causes of hypoglycemia. The most frequently found adverse drug reactions in the study by Shareef et al¹⁵ were hypoglycemia in 65 (63.72%). It is generally understood that anti-diabetic medications can cause hypoglycemia. Several studies have reported cases of low blood sugar attributed to insulin and sulfonylureas, and they have identified hypoglycemia as one of the major reasons why patients with diabetes mellitus are admitted to hospitals for medical reasons.¹⁶⁻¹⁸ In a Danish research by Hallas et al¹⁹ hypoglycemia linked to insulin usage was a factor in 14 out of 157 hospitalizations. In two research studies from Hong Kong^{20,21}, where diabetes mellitus is prevalent, greater incidences of hypoglycemia were associated with sulfonylurea use. According to the prospective research conducted in Sicily²², 11% of all individuals with diabetes mellitus experienced adverse drug reactions.

Males ($n=13$) were found to have a higher incidence of ADRs than females ($n=6$). The research of Rao et al²³ as well as Dilip et al²⁴ supports the preponderance of men. The majority of ADRs ($n=14$) were detected in the older age group. According to a number of studies conducted by Pirmohamed et al²⁵, and Arain et al²⁶, the proportion of ADRs observed in the adult population was greater.

CONCLUSION

Adverse drug resistances are a concern for medication safety and are one of the drug-related issues that are thought to be a major factor in hospital-related admissions. It is crucial to monitor ADRs in patients on anti-diabetic medications because it is known to lead to hypoglycemia. A greater frequency of ADRs was related with older age, male gender, as well as diabetes duration of longer than 5 years. The findings of this study inform healthcare professionals about the significance of tracking and disclosing adverse drug reactions particularly in older individuals with hyperglycemia who may experience serious adverse drug reactions. A better patient outcome would result from the clinical pharmacist's active participation in ADR's detection, monitoring, and treatment through therapeutic intervention.

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