World Journal of Pharmaceutical Science and Research

www.wjpsronline.com

Research Article

ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 8
Page: 820-830

REAL-WORLD SAFETY PROFILE OF TIRZEPATIDE: A DESCRIPTIVE ANALYSIS OF THE FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

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Article Received: 01 July 2026 | | ***Article Revised: 22 July 2026*** | | ***Article Accepted: 12 August 2026***

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DOI: https://doi.org/10.5281/zenodo.21949710

How to cite this Article: Mukthiyar Ahamed, Irfan (2026) REAL-WORLD SAFETY PROFILE OF TIRZEPATIDE: A DESCRIPTIVE ANALYSIS OF THE FDA ADVERSE EVENT REPORTING SYSTEM (FAERS). World Journal of Pharmaceutical Science and Research, 5(8), 820-830.

ABSTRACT

Background: Tirzepatide is a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist approved for the management of type 2 diabetes mellitus and obesity. Although clinical trials have demonstrated its efficacy and acceptable safety profile, continuous post-marketing surveillance is essential to identify adverse drug reactions reported during routine clinical use. Real-world pharmacovigilance databases provide valuable information for monitoring the safety of newly introduced medicines across diverse patient populations. **Objectives:** The present study aimed to evaluate the real-world safety profile of tirzepatide by analyzing adverse event reports available in the United States Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). **Materials and Methods:** A retrospective descriptive pharmacovigilance study was conducted using publicly available reports from the FAERS database. Reports in which tirzepatide was recorded as a suspected drug were included in the analysis. Demographic characteristics, reporter type, frequently reported adverse events, and System Organ Class (SOC) distributions were evaluated using descriptive statistical methods. **Results:** A total of 158,914 adverse event reports associated with tirzepatide were identified. Among these, 27,118 were classified as serious cases and 821 reported deaths as an outcome. Adults aged 18–64 years represented the largest patient group. Female patients accounted for 61.07% of the reports, while consumers submitted the majority of reports (93.02%). Frequently reported clinical adverse events included nausea, injection-site pain, diarrhoea, vomiting, constipation, abdominal pain, fatigue, and headache. System Organ Class analysis showed that General Disorders and Administration Site Conditions, Gastrointestinal Disorders, and Injury, Poisoning and Procedural Complications were among the most frequently reported categories. **Conclusion:** The findings provide valuable real-world evidence regarding the safety profile of tirzepatide in routine clinical practice. Gastrointestinal symptoms and injection-site reactions were among the most frequently reported adverse events. Continuous pharmacovigilance and careful monitoring of patients receiving tirzepatide remain important to support its safe and effective clinical use.

KEYWORDS: Tirzepatide, FAERS, Pharmacovigilance, Adverse Drug Reactions, Drug Safety, Real-World Evidence, Type 2 Diabetes Mellitus, Obesity.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and obesity are major public health concerns that have increased substantially over the past few decades. Both conditions are associated with an elevated risk of cardiovascular disease, chronic kidney disease, non-alcoholic fatty liver disease, and reduced quality of life. According to the International Diabetes Federation (IDF), the global prevalence of diabetes continues to rise, placing a significant burden on healthcare systems and emphasizing the need for effective therapeutic strategies. In addition to controlling blood glucose levels, modern treatment approaches aim to reduce body weight, improve metabolic health, and minimize long-term complications.[1,2]

Tirzepatide is a novel once-weekly injectable medication that has attracted considerable attention because of its dual mechanism of action. Unlike conventional glucagon-like peptide-1 (GLP-1) receptor agonists, tirzepatide activates both the glucose-dependent insulinotropic polypeptide (GIP) receptor and the GLP-1 receptor. This dual incretin activity enhances glucose-dependent insulin secretion, suppresses glucagon release, delays gastric emptying, and promotes satiety, resulting in improved glycaemic control and clinically significant weight reduction. Based on evidence from large clinical trials, tirzepatide has been approved for the treatment of type 2 diabetes mellitus, and its therapeutic role has expanded in obesity management in several countries.[3]

Although randomized clinical trials provide essential evidence regarding the efficacy and safety of newly approved medicines, they are performed under controlled conditions with predefined eligibility criteria and limited follow-up periods.[4] Consequently, rare adverse drug reactions, delayed events, and reactions occurring in specific patient populations may not be fully identified before marketing approval. As the use of tirzepatide continues to increase in routine clinical practice, continuous monitoring of its safety profile has become increasingly important.[5,7]

Pharmacovigilance plays a vital role in ensuring the safe use of medicines after they become available to the public. It involves the systematic collection, evaluation, and interpretation of adverse drug reaction reports to identify potential safety concerns that may not have been detected during clinical development. Post-marketing surveillance contributes to improved patient care by supporting regulatory decision-making, updating prescribing information, and identifying previously unrecognized adverse events.[8,10]

The United States Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) is one of the world's largest spontaneous reporting databases for monitoring medicine safety.[11] The database contains millions of Individual Case Safety Reports submitted by healthcare professionals, pharmaceutical manufacturers, and consumers. Although spontaneous reporting systems cannot establish a causal relationship between a drug and an adverse event, they provide valuable real-world evidence regarding the pattern and frequency of reported reactions across diverse patient populations.[20]

Previous clinical studies have shown that gastrointestinal adverse events such as nausea, vomiting, diarrhoea, and constipation are commonly associated with tirzepatide therapy. However, real-world reporting may also identify additional adverse events, administration-related reactions, or uncommon safety concerns that deserve further evaluation. Descriptive analysis of FAERS data helps characterize these reported events and provides an overview of the post-marketing safety experience with the drug.[6]

Therefore, the present study was conducted to evaluate the real-world safety profile of tirzepatide using reports available in the FDA Adverse Event Reporting System (FAERS). The study describes patient demographics, reporter characteristics, frequently reported adverse events, and System Organ Class distributions to provide a comprehensive overview of adverse events reported during routine clinical use. The findings are expected to contribute additional real-world evidence that may support clinicians, researchers, and regulatory authorities in understanding the post-marketing safety profile of tirzepatide.[9]

MATERIALS AND METHODS

Study Design

The present study was designed as a retrospective descriptive pharmacovigilance investigation to evaluate the safety profile of tirzepatide using spontaneous adverse event reports from the FDA Adverse Event Reporting System (FAERS).[9]

Data Source

Adverse event reports were obtained from the FDA Adverse Event Reporting System (FAERS), a publicly available pharmacovigilance database maintained by the United States Food and Drug Administration (FDA). The database contains Individual Case Safety Reports (ICSRs) submitted by healthcare professionals, pharmaceutical companies, consumers, and other reporters worldwide.

Study Period

FAERS reports involving tirzepatide were collected from May 2022 (FDA approval) through the most recent quarter available at the time of data extraction.

Inclusion Criteria

1. Reports listing tirzepatide as the Primary Suspect (PS) drug.
2. Reports listing tirzepatide as the Secondary Suspect (SS) drug.
3. Reports containing complete information on adverse events and patient characteristics.

Exclusion Criteria

1. Duplicate reports.
2. Reports with incomplete or missing essential information.
3. Reports in which tirzepatide was not identified as a suspected drug.
4. Invalid or incorrectly entered reports.

Data Extraction

The following variables were extracted from the FAERS database:

- Patient age
- Patient sex
- Country of report
- Reporter type
- Year of reporting
- Seriousness of the event

- Clinical outcome (death, hospitalization, disability, life-threatening event, etc.)
- Reported adverse drug reactions (Preferred Terms)
- System Organ Class (SOC)
- Suspected drug information

Statistical Analysis

Descriptive statistical analysis was performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). Categorical variables were summarized as frequencies and percentages. The results were presented using tables and graphical representations to describe the distribution of adverse event reports associated with tirzepatide.[12]

Classification of Adverse Drug Reactions

Adverse drug reactions were classified according to the Medical Dictionary for Regulatory Activities (MedDRA) terminology and grouped into their respective System Organ Classes (SOCs).[14,18]

Descriptive Analysis

Descriptive statistical analysis was performed to summarize:

- Age-wise distribution of reports
- Sex-wise distribution
- Reporter type
- Year-wise reporting trend
- Serious versus non-serious reports
- Most frequently reported adverse drug reactions
- Distribution of reports across System Organ Classes

Ethical Considerations

The study utilized publicly available, de-identified data from the FDA Adverse Event Reporting System (FAERS). Since no patient-identifiable information was accessed, institutional ethics committee approval and informed consent were not required.

RESULTS

Overall Distribution of Adverse Event Reports

A total of 158,914 adverse event reports associated with tirzepatide were identified in the FDA Adverse Event Reporting System (FAERS) during the study period. Among these reports, 27,118 were classified as serious adverse events, while 821 reports had death recorded as the clinical outcome. These findings indicate that most reported events were non-serious, although a substantial number of serious cases were also documented.

Age-wise Distribution of Adverse Event Reports

Adults aged 18–64 years represented the largest proportion of reported cases, accounting for 78,577 reports (49.45%). Patients aged 65–85 years contributed 28,877 reports (18.17%), whereas 51,108 reports (32.16%) did not contain age information.

Table 1: Age-wise Distribution of Adverse Event Reports.

Age Group	Number of Reports	Percentage (%)
18–64 years	78,577	49.45
65–85 years	28,877	18.17
Age not specified	51,108	32.16
Total	**158,914**	**100.00**

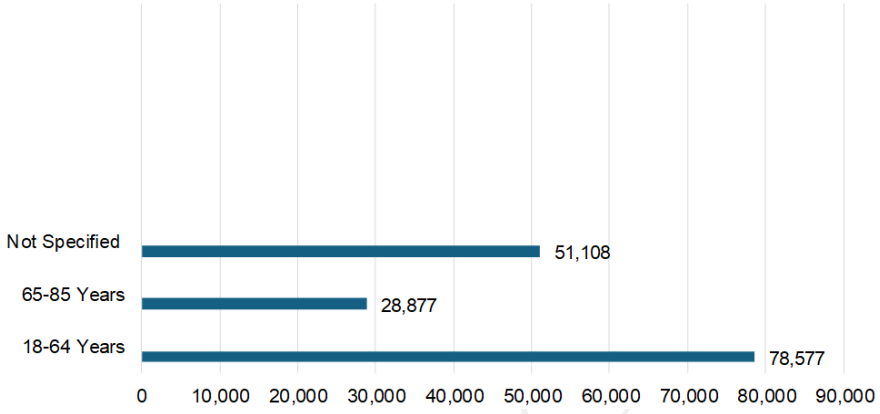

Figure 1: Age-wise distribution of adverse event reports associated with tirzepatide reported in the FDA Adverse Event Reporting System (FAERS).

Sex-wise Distribution of Adverse Event Reports

Female patients accounted for the majority of adverse event reports (97,054; 61.07%), followed by male patients (30,666; 19.30%). Sex was not specified in 31,194 reports (19.63%).

Table 2: Sex-wise Distribution of Adverse Event Reports.

Sex	Number of Reports	Percentage (%)
Female	97,054	61.07
Male	30,666	19.30
Not Specified	31,194	19.63
Total	**158,914**	**100.00**

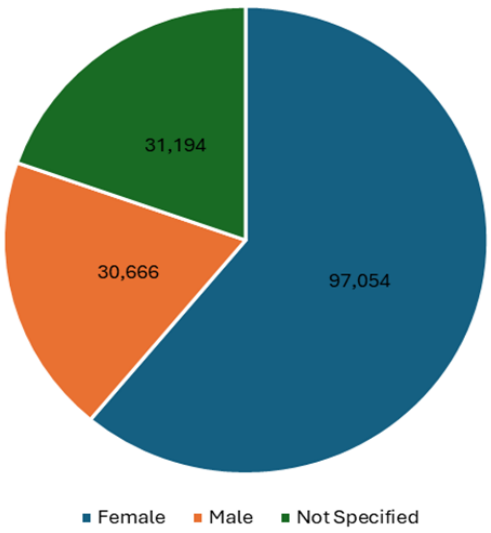

Figure 2: Sex-wise distribution of adverse event reports associated with tirzepatide reported in the FDA Adverse Event Reporting System (FAERS).

Year-wise Distribution of Adverse Event Reports

The number of adverse event reports associated with tirzepatide increased progressively following its approval. A total of 3,124 reports (1.97%) were received in 2022, increasing to 15,904 (10.01%) in 2023 and 37,405 (23.54%) in 2024. The highest number of reports was recorded in 2025 (58,994; 37.12%), followed by 43,487 reports (27.37%) in 2026.

Table 3: Year-wise Distribution of Adverse Event Reports.

Received Year	Number of Reports	Percentage (%)
2022	3,124	1.97
2023	15,904	10.01
2024	37,405	23.54
2025	58,994	37.12
2026	43487	27.37
Total	**158,914**	**100.00**

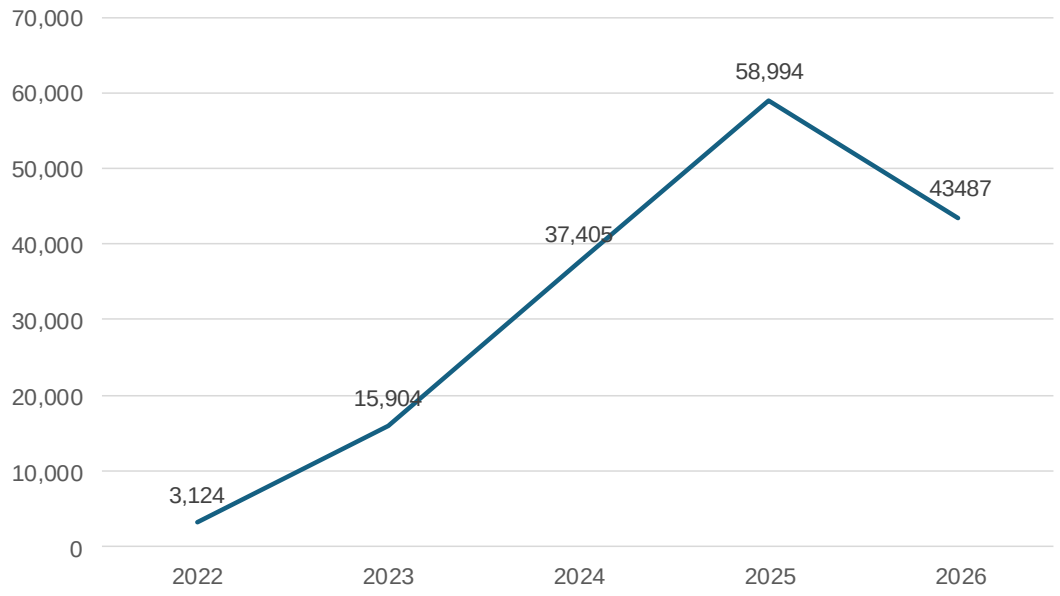

Figure 3: Year-wise distribution of adverse event reports associated with tirzepatide reported in the FDA Adverse Event Reporting System (FAERS).

Reporter Type Distribution

Consumers were responsible for the majority of adverse event reports (**147,815; 93.02%**). Healthcare professionals submitted **10,963 reports (6.90%)**, while reports from other sources or with unspecified reporter type represented only a small proportion of the total.

Table 4: Reporter Type Distribution.

Reporter type	Number of reports	Percentage%
Consumer	147,815	93.02
Healthcare Professional	10,963	6.90
Other	20	0.01
Not Specified	116	0.07
Total	158,914	100.00

Frequently Reported Adverse Drug Reactions

Among the clinically relevant reported adverse events, nausea was the most frequently reported reaction, followed by injection site pain, diarrhoea, vomiting, and constipation. Other commonly reported adverse events included fatigue, headache, decreased appetite, dyspepsia, and dizziness.

Table 5: Frequently Reported Adverse Drug Reactions

Adverse Drug Reactions	Number of Reports	Percentage %
Nausea	17,409	10.95
Injection site pain	13,663	8.60
Diarrhoea	10,056	6.33
Vomiting	8,398	5.28
Constipation	6,698	4.21
Injection Site haemorrhage	5,278	3.32
Injection Site erythema	5,247	3.30
Fatigue	4,530	2.85
Upper abdominal pain	3,739	2.35
Headache	3,187	2.01

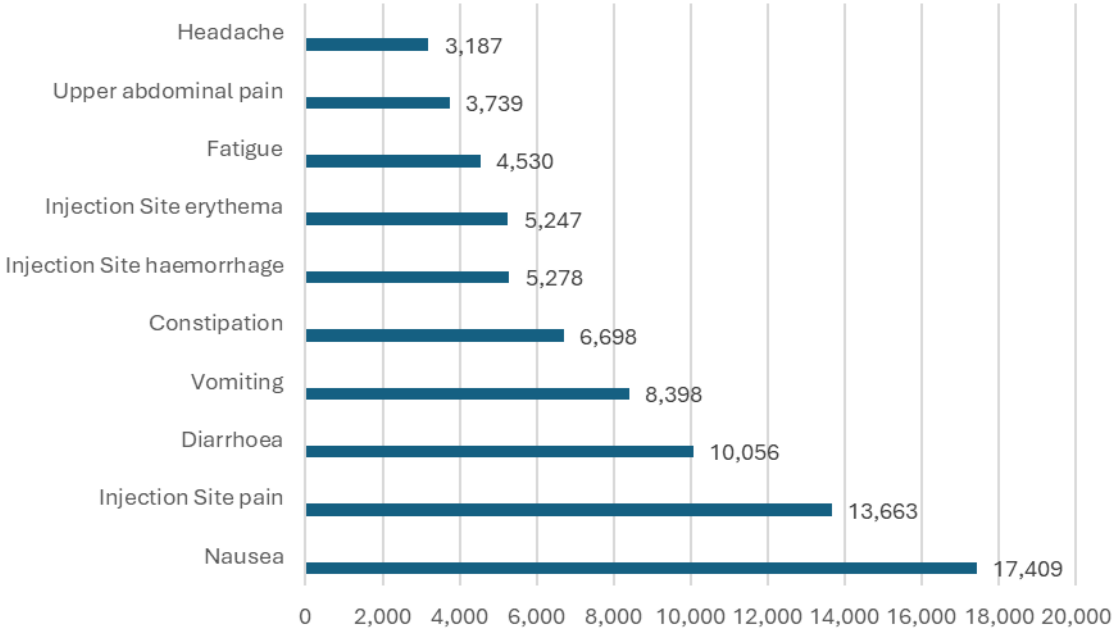

Figure 4: Top reported adverse drug reactions associated with tirzepatide reported in the FDA Adverse Event Reporting System (FAERS).

System Organ Class Distribution

Adverse events were categorized according to the Medical Dictionary for Regulatory Activities (MedDRA) System Organ Classes (SOCs). The largest number of reports belonged to Injury, Poisoning and Procedural Complications, followed by General Disorders and Administration Site Conditions and Gastrointestinal Disorders.

Table 6: System Organ Class Distribution.

System Organ Class	Number of Reports
Injury, Poisoning and Procedural Complications	65,296
General Disorders and Administration Site Conditions	58,875
Gastrointestinal Disorders	42,583

Investigations	14,084
Nervous System Disorders	12,129
Metabolism and Nutrition Disorder	10,320
Skin and Subcutaneous Tissue Disorders	7,523
Psychiatric Disorders	6,589

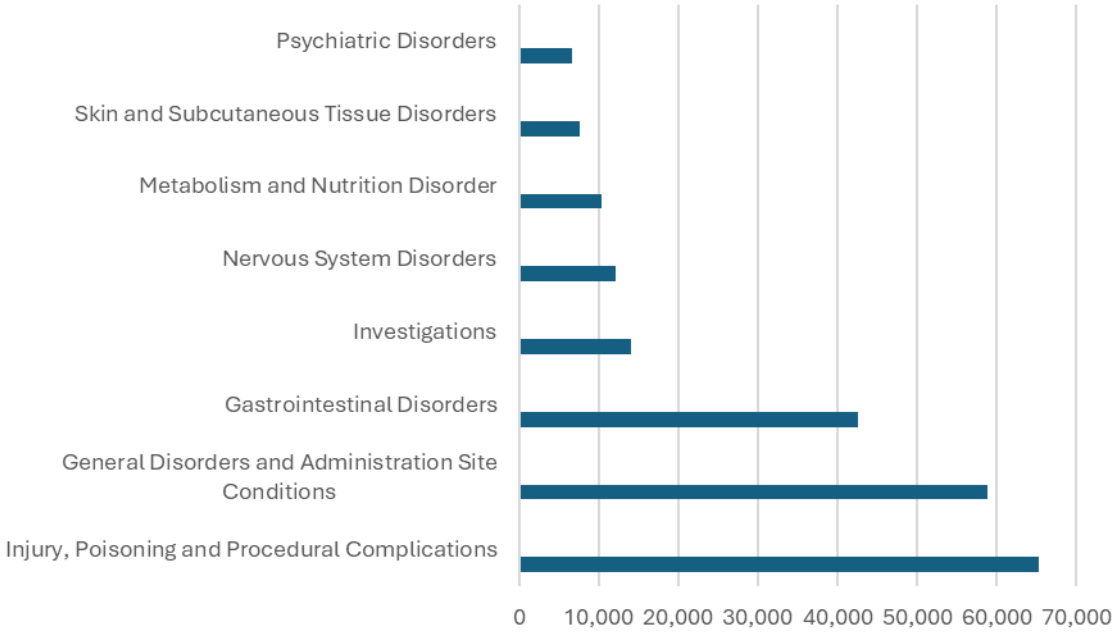

Figure 5: Distribution of adverse event reports associated with tirzepatide according to MedDRA System Organ Class (SOC) reported in the FDA Adverse Event Reporting System (FAERS).

DISCUSSION

The present study evaluated the post-marketing safety profile of tirzepatide using adverse event reports available in the FDA Adverse Event Reporting System (FAERS). Analysis of 158,914 reports provided an overview of the demographic characteristics of affected patients, reporter categories, frequently reported adverse events, and the distribution of adverse events across different System Organ Classes.[2,3] The findings contribute to the growing body of real-world evidence regarding the safety of tirzepatide in routine clinical practice.[5]

A substantial proportion of reports involved adults aged 18–64 years, which is expected because tirzepatide is primarily prescribed to adults with type 2 diabetes mellitus and obesity. Female patients accounted for more than half of all reported cases. This observation may reflect differences in prescribing patterns, healthcare-seeking behavior, or adverse event reporting between males and females. However, the FAERS database does not contain exposure data; therefore, it is not possible to determine whether females have a higher risk of adverse events or simply represent a larger proportion of tirzepatide users.[16,19]

The majority of reports were submitted by consumers rather than healthcare professionals. This finding highlights the increasing role of patient-reported outcomes in post-marketing pharmacovigilance. Consumer reports provide valuable real-world information regarding medicine safety, although they may vary in completeness and clinical detail compared with reports submitted by healthcare professionals.[15]

Among the reported adverse events, gastrointestinal symptoms such as nausea, diarrhoea, vomiting, constipation, dyspepsia, and upper abdominal pain were frequently observed. These findings are consistent with the known pharmacological effects of tirzepatide. By activating GIP and GLP-1 receptors, tirzepatide delays gastric emptying and influences gastrointestinal motility, which may contribute to the occurrence of these symptoms. Most gastrointestinal adverse events reported with incretin-based therapies are generally mild to moderate in severity and often improve with continued treatment or gradual dose escalation.

Injection-site reactions, including pain, erythema, haemorrhage, and pruritus, were also commonly reported. Since tirzepatide is administered by subcutaneous injection, local reactions at the injection site are expected in a proportion of patients. Appropriate injection techniques and rotation of injection sites may help reduce these reactions during long-term therapy.[18,20]

System Organ Class analysis demonstrated that General Disorders and Administration Site Conditions and Gastrointestinal Disorders represented a large proportion of reported adverse events. This distribution is consistent with the reaction-level findings and reflects the expected safety profile of tirzepatide observed in both clinical studies and post-marketing reports.

Although the FAERS database is an important resource for pharmacovigilance, several limitations should be considered when interpreting the findings. FAERS is a spontaneous reporting system and is subject to under-reporting, duplicate reports, reporting bias, and incomplete clinical information. In addition, the database does not provide the total number of patients exposed to tirzepatide, making it impossible to estimate the incidence or prevalence of adverse events. Furthermore, the descriptive nature of this study does not establish a causal relationship between tirzepatide and the reported adverse events.

Despite these limitations, the present study provides useful real-world information regarding the post-marketing safety profile of tirzepatide. Continuous pharmacovigilance and careful monitoring of adverse events remain important to improve patient safety and support evidence-based clinical decision-making.[12,17]

CONCLUSION

The present study provides a comprehensive overview of the real-world safety profile of tirzepatide using adverse event reports retrieved from the FDA Adverse Event Reporting System (FAERS). Analysis of 158,914 reports demonstrated that gastrointestinal disorders and injection-site reactions were among the most frequently reported adverse events. Adults aged 18–64 years accounted for the largest proportion of reports, and female patients represented the majority of reported cases. Consumer reports constituted the largest source of adverse event submissions, highlighting the growing contribution of patients to post-marketing pharmacovigilance.

Overall, the findings are consistent with the known safety profile of tirzepatide observed in clinical practice. Continuous monitoring of adverse events through spontaneous reporting systems remains essential for identifying emerging safety concerns and supporting informed clinical decision-making. Further analytical and pharmacoepidemiological studies are warranted to better characterize the long-term safety profile of tirzepatide and to evaluate potential risk factors associated with specific adverse events.

LIMITATIONS

The present study has several limitations that should be considered while interpreting the findings.

1. The FAERS database is a spontaneous reporting system and is therefore subject to under-reporting and reporting bias.
2. The quality and completeness of adverse event reports vary among reporters, which may influence the accuracy of the available information.
3. The database does not contain the total number of patients exposed to tirzepatide; therefore, the incidence and prevalence of adverse events cannot be determined.
4. A causal relationship between tirzepatide and the reported adverse events cannot be established solely from spontaneous reports.
5. Clinical information such as disease severity, treatment duration, dosage adjustments, concomitant medications, and laboratory findings is often incomplete or unavailable.
6. The present study is descriptive in nature and summarizes reported adverse events without estimating comparative risk.

FUTURE SCOPE

Future studies may further improve the understanding of tirzepatide safety by:

1. Conducting disproportionality analyses using PRR, ROR, Information Component (IC), or Empirical Bayes methods to identify potential safety signals.
2. Comparing the safety profile of tirzepatide with other GLP-1 receptor agonists and dual incretin therapies.
3. Evaluating long-term adverse events using multiple pharmacovigilance databases such as FAERS, EudraVigilance, and VigiBase.
4. Investigating adverse events in specific patient populations, including elderly patients, individuals with renal impairment, and patients receiving combination therapy.
5. Performing prospective observational studies to validate findings obtained from spontaneous reporting systems.

FUNDING

The authors declare that no external funding was received for conducting this study.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

DATA AVAILABILITY STATEMENT

The data used in this study were obtained from the publicly accessible FDA Adverse Event Reporting System (FAERS). Additional information can be accessed through the FDA FAERS Public Dashboard.

ETHICAL STATEMENT

The study utilized publicly available, anonymized adverse event reports from the FDA Adverse Event Reporting System (FAERS). As no patient-identifiable information was used, ethical committee approval and informed consent were not required.

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