Real-World Adverse Drug Reactions to Semaglutide: A Case Series from an Indian Tertiary Care Centre

[1]Anu V. Babu, [2]Manish Mohan M, [1]Devi V. S, [3]Swetha Reba Mathews, [2]Jacob Jesurun R. S

[1] Department of Surgery, Sree Gokulam Medical College & Research Foundation, Venjaramoodu, Thiruvananthapuram, Kerala, India

[2] Department of Pharmacology, Believers Church Medical College Hospital, Thiruvalla, Kerala, India

[3] Departments of Pharmacology, Sree Gokulam Medical College & Research Foundation, Venjaramoodu, Thiruvananthapuram, Kerala, India

Corresponding author: **Dr. Manish Mohan M**

Abstract: Background: Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), is increasingly prescribed for the management of type 2 diabetes mellitus and obesity owing to its proven efficacy in glycogenic control and weight reduction. However, with expanding use, a broader spectrum of adverse drug reactions (ADRs)—ranging from common gastrointestinal intolerance to rare but clinically significant complications—has been increasingly recognized, underscoring the need for continued real-world pharmacovigilance. **Objective:** To describe a case series of semaglutide-associated ADRs reported from a tertiary care centre in India, highlighting the variability in clinical presentation, the role of uniform baseline investigations, and the importance of comprehensive medication history in causality assessment. **Methods:** Five patients receiving semaglutide for type 2 diabetes mellitus (n = 3) or obesity (n = 2) developed clinically significant ADRs. All cases underwent uniform baseline and follow-up investigations, including complete blood count, liver and renal function tests, serum electrolytes, and glycogenic parameters (HbA1c/fasting plasma glucose). Detailed drug histories, co morbidities, and concomitant medications were systematically reviewed. Causality assessment was performed using the WHO–UMC criteria. **Results:** The documented ADRs comprised generalized pruritus (n = 1), severe nausea and vomiting (n = 2), acute kidney injury (n = 1), and gastro paresis-like symptoms (n = 1). All reactions demonstrated a clear temporal relationship with semaglutide initiation or dose escalation and were categorized as probable on WHO–UMC causality assessment. Alternative aetiologies, including concomitant medications and underlying comorbidities, were reasonably excluded. Clinical improvement and complete resolution of symptoms were observed in all patients following discontinuation and appropriate supportive management. **Conclusion:** Although semaglutide is an effective and widely used therapeutic agent, this case series highlights the occurrence of clinically relevant ADRs in routine clinical practice within an Indian tertiary care setting. The findings reinforce the importance of uniform baseline evaluation, cautious dose titration, meticulous medication history, and proactive pharma covigilance reporting through the Pharma covigilance Programme of India (PvPI) to enhance patient safety and sustain therapeutic confidence.

Keywords: Semaglutide; GLP-1 receptor agonist; Adverse drug reactions; Pharmacovigilance; Case series; WHO-UMC causality

Introduction:

Semaglutide is a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist approved for the management of type 2 diabetes mellitus (T2DM) and obesity. It mimics endogenous GLP-1 activity by promoting glucose-dependent insulin secretion, suppressing glucagon release, delaying gastric emptying, and enhancing satiety [1]. Landmark clinical trials such as SUSTAIN and STEP have demonstrated its significant benefits in glycolic control and weight reduction [2].

Despite these advantages, semaglutide is not without adverse effects. Gastrointestinal symptoms—particularly nausea, vomiting, and diarrhea—are the most frequently observed, especially during dose escalation [4]. Rare but clinically significant adverse reactions, including acute kidney injury (AKI), dermatologic hypersensitivity, and neuropsychiatric effects such as depression, have also been reported in limited numbers [3,5,7]. With the increasing use of semaglutide, particularly in non-diabetic populations, post-marketing surveillance and detailed case documentation are essential to inform clinical practice and ensure patient safety.

This case series contributes to the pharmacovigilance literature by describing five cases of semaglutide-associated ADRs reported to the Pharmacovigilance Programmed of India (PvPI). Although these ADRs are recognized, their rare documentation in real-world Indian patients—across both obesity and diabetes indications—highlights the importance of systematic monitoring, uniform baseline investigations, and comprehensive medication history documentation. Furthermore, structured causality assessment using WHO-UMC criteria strengthens attribution of these ADRs to semaglutide and reinforces the role of case series in pharmacovigilance practice.

Methodology

This case series includes five patients who developed adverse drug reactions (ADRs) following semaglutide therapy for either type 2 diabetes mellitus or obesity at a tertiary care centre. Detailed clinical histories, comorbidities, and concomitant medication use were recorded for each patient. Uniform baseline investigations, including complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), serum electrolytes, and HbA1c or fasting glucose, were performed to ensure comparability across cases. Additional investigations (e.g., urinalysis, upper GI endoscopy) were conducted where clinically indicated.

Causality assessment was conducted using the **World Health Organisation–Uppsala Monitoring Centre (WHO-UMC) criteria**. Each ADR was evaluated for temporal association with drug initiation, dose, and duration, dechallenge response (resolution upon drug withdrawal), exclusion of alternative etiologies, and the presence or absence of rechallenge. Based on these factors, causality was categorised as probable in all cases. This

structured approach ensured uniformity, minimised bias, and provided stronger attribution of the observed ADRs to semaglutide.

Case Series

Case 1 – Semaglutide-Induced Pruritus

A 53-year-old male with type 2 diabetes mellitus, receiving semaglutide 0.25 mg weekly as an add-on to metformin and glimepiride, developed generalised pruritus within five days of therapy initiation. There was no rash, angioedema, or systemic symptoms. Baseline investigations (CBC, LFT, RFT, electrolytes, HbA1c) were normal. The ADR was recognised early, and semaglutide was discontinued. The patient was treated with oral antihistamines, which provided partial relief. Pruritus subsided completely within two weeks of drug withdrawal, and no recurrence was noted on follow-up. WHO-UMC Causality Assessment: Probable

Case 2 – Severe Nausea and Vomiting

A 45-year-old female prescribed semaglutide (0.5 mg weekly) for weight loss developed severe nausea and intractable vomiting after her second dose. She presented with dehydration and weakness. Baseline labs (CBC, LFT, RFT, electrolytes, fasting glucose) were normal, but repeat investigations revealed mild hypokalemia (serum K^+: 3.2 mmol/L). Semaglutide was immediately discontinued. She was admitted and treated with intravenous fluids, antiemetic, and potassium correction. Symptoms improved significantly within 48 hours, and she was discharged in stable condition. On follow-up, she remained symptom-free with no recurrence. WHO-UMC Causality Assessment: Probable

Case 3 – Acute Kidney Injury (AKI)A 44-year-old female without prior renal disease initiated semaglutide 0.5 mg weekly for diabetes management. On day 10, she developed fatigue, oliguria, and peripheral oedema. Baseline labs (CBC, LFT, RFT, HbA1c, electrolytes) were normal. At presentation, serum creatinine had increased to 2.4 mg/dL, with a bland urinalysis. No concomitant nephrotoxic medications or alternative causes were identified. Semaglutide was discontinued, and the patient received intravenous fluids and supportive care. Renal function gradually normalized within 7 days of withdrawal, with serum creatinine returning to baseline (1.0 mg/dL). She was monitored for three months without recurrence. WHO-UMC Causality Assessment: Probable

Case 4 – Gastrointestinal Distress (Gastroparesis-like Symptoms)

A 67-year-old male with type 2 diabetes, on metformin and amlodipine, was initiated on semaglutide. After 4 weeks of therapy, he reported persistent bloating, early satiety, and unintentional weight loss. Baseline labs (CBC, LFT, RFT, HbA1c, electrolytes) were

normal. Upper GI endoscopy and abdominal imaging ruled out obstructive pathology. On recognition of ADR, semaglutide was stopped. He was managed conservatively with dietary modification, prokinetic agents, and hydration. Symptoms resolved within 10 days of drug cessation. Weight stabilised over the next month, and no further GI complaints were reported. WHO-UMC Causality Assessment: Probable

Case 5 – Severe Nausea

A 42-year-old woman with obesity received her first dose of semaglutide (0.25 mg weekly). Within 48 hours, she developed severe nausea, anorexia, and an inability to tolerate oral intake. Baseline investigations (CBC, LFT, RFT, electrolytes, fasting glucose) were normal, and no comorbidities or concomitant medications were present. Semaglutide was promptly discontinued, and she was managed with oral rehydration and antiemetics. Symptoms resolved fully within 5 days, with appetite returning to baseline. She remained well on follow-up, and no alternative anti-obesity pharmacotherapy was initiated.

WHO-UMC Causality Assessment: Probable

Table No: 1 Case Series Summary

Case No.	Age/Sex	ADR Type	Key Investigations	Representative Values	Findings	Causality (WHO-UMC)
1	53 / M	Generalized purities	LFT	AST: 28 U/L ALT: 32 U/L ALP: 96 U/L Total bilirubin: 0.8 mg/dL	Normal LFT	Probable
			RFT	Serum creatinine: 0.9 mg/dL Blood urea: 26 mg/dL	Normal renal function	
			CBC	Hb: 14.2 g/dL TLC: 6,800 /µL Platelets: 2.4 $\times 10^5$ /µL	Normal CBC	

2	45 / F	Severe nausea & vomiting	Serum electrolytes	Na^+: 138 mmol/L K^+: 3.1 mmol/L Cl^-: 101 mmol/L	Mild hypokalemia	Probable
			RFT	Serum creatinine: 0.8 mg/dL	Normal	
3	44 / F	Acute kidney injury	Serum creatinine	2.4 mg/dL (baseline ~0.9 mg/dL)	AKI	Probable
			Blood urea	68 mg/dL	Elevated	
			Urinalysis	Protein: Nil RBC: 0–1 /HPF Casts: Absent	Bland urine sediment	
4	67 / M	Gastro paresis-like symptoms	Upper GI endoscopy	Normal mucosa, no ulcer/stricture	No mechanical cause	Probable
			Abdominal imaging (USG/CT)	Normal stomach & bowel loops	No obstruction	
			Basic labs	Hb: 13.1 g/dL Creatinine: 1.0 mg/dL	Normal	
5	42 / F	Severe nausea	CBC	Hb: 12.6 g/dL TLC: 7,200 /µL Platelets: 2.6 $\times 10^5$ /µL	Normal	Probable
			LFT	AST: 26 U/L ALT: 30 U/L Bilirubin: 0.7 mg/dL	Normal	
			RFT	Serum creatinine: 0.85 mg/dL	Normal	

Discussion

This case series provides real-world evidence of semaglutide-associated adverse drug reactions (ADRs) in patients treated for both type 2 diabetes mellitus and obesity. The spectrum of ADRs observed included gastrointestinal events (nausea, vomiting, and gastro paresis-like symptoms), dermatological manifestations (generalized purities), and acute kidney injury (AKI). Gastrointestinal intolerance is the most frequently reported adverse effect of semaglutide and is primarily related to its pharmacodynamic properties, namely delayed gastric emptying and central appetite suppression mediated via glucagon-like peptide-1 receptor activation. However, the present cases highlight that the severity of gastrointestinal symptoms can range from mild, self-limiting nausea to persistent symptoms necessitating clinical evaluation or hospitalization. Such intolerance may adversely impact treatment adherence and limit long-term therapy, particularly when dose escalation is rapid or patient susceptibility is underestimated. These findings are concordant with existing literature, wherein GLP-1 receptor agonist–induced gastrointestinal effects have been shown, in certain cases, to mimic or precipitate gastro paresis-like presentations [6].

A clinically significant finding in this series was the occurrence of AKI, an uncommon but potentially serious ADR associated with semaglutide. The mechanism underlying renal dysfunction is likely multi factorial, with volume depletion secondary to prolonged nausea and vomiting being the predominant contributor rather than direct nephrotoxicity. This observation is supported by the presence of bland urine sediment and the absence of obstructive pathology or intrinsic renal disease on evaluation. These findings underscore the need for cautious use of semaglutide in susceptible populations, including elderly patients, those with pre-existing renal impairment, or individuals exposed to concurrent nephrotoxic agents, and reinforce the importance of periodic renal function monitoring during therapy [5].

Generalized purities without accompanying biochemical or systemic abnormalities was another notable but rare ADR observed in this series. Although infrequently reported, dermatological reactions to semaglutide may represent immune-mediated hypersensitivity responses. Early recognition of such reactions is essential, as prompt drug discontinuation generally leads to symptom resolution and prevents progression to more severe hypersensitivity manifestations [3]. Clinicians should therefore maintain a high index of suspicion when unexplained pruritus develops following initiation of therapy.

Beyond the commonly recognized gastrointestinal and renal adverse effects, emerging evidence has suggested potential neuropsychiatric associations with semaglutide, including depressive symptoms. While such events were not observed in the present series, isolated reports in the literature highlight the need for ongoing vigilance,

particularly in patients with underlying psychiatric vulnerability or during prolonged treatment courses [7].

The temporal relationship between drug exposure and symptom onset, consistent improvement following drug withdrawal, absence of alternative etiologies and favorable clinical outcomes collectively strengthen the causal association between semaglutide and the observed ADRs. Management strategies—including symptomatic treatment with antihistamines for dermatological reactions, fluid and electrolyte correction for gastrointestinal intolerance, and supportive care for AKI—were effective, with all patients demonstrating complete clinical recovery.

In conclusion, while semaglutide remains a highly effective and widely utilized therapy for glycaemic control and weight reduction, clinicians must remain vigilant for both common and rare ADRs. Uniform baseline evaluation, gradual dose titration, proactive patient counseling regarding early warning symptoms, and systematic pharmacovigilance reporting are essential to maximize therapeutic benefit while minimizing preventable harm.

Conclusion

Semaglutide is an effective therapy for diabetes and obesity, but may cause adverse reactions ranging from common gastrointestinal intolerance to rare events such as acute kidney injury and dermatological hypersensitivity. In this series, all reactions resolved with timely recognition, discontinuation, and supportive care, emphasizing the need for vigilance in clinical practice. Uniform baseline investigations, gradual dose titration, review of concomitant medications, and pharmacovigilance reporting are essential to optimize therapeutic benefit while ensuring patient safety.

Funding: The authors received no financial support for the research, authorship, and/or publication of this case series.

Conflict of Interest: The authors declare no conflicts of interest related to this work.

References

1. **Marso SP, Bain SC, Consoli A, et al.** Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med.* 2016;375(19):1834–1844.
2. **Wilding JPH, Batter ham RL, Calanna S, et al.** Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med.* 2021;384(11):989–1002.
3. **Ouellette S, Frias G, Shah R, et al.** Dermal hypersensitivity reaction to semaglutide: two case reports. *J Drugs Dermatol.* 2023;22(4):413–415.

4. **Zhang Y, Liu J, Wang Y, et al.** Gastrointestinal adverse events associated with semaglutide: a pharmacovigilance study based on the FDA adverse event reporting system. *Front Pharmacol.* 2022;13:963144.
5. **Momen NC, Plana-Ripoll O, Agerbo E, et al.** Disproportionality analysis from WHO data on semaglutide and suicidality. *JAMA Netw Open.* 2023;6(12):e2339450.
6. **Khan MA, Patel K, Shah A, et al.** Tendency of semaglutide to induce gastroparesis: a case report. *Clin Diabetes Endocrinol.* 2024; 10: Article ID 38371020.
7. **Li Y, Cao Y, Wei Y, Geng D.** Semaglutide-associated depression: a report of two cases. *Front Psychiatry.* 2023; 14:1238353