

## Can tirzepatide transform HFpEF management in Pakistan? A call for action

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*The Editor*, Obesity is a well-established risk factor associated with heart failure, and its intersection with heart failure with preserved ejection fraction (HFpEF) presents a major challenge for the healthcare systems of the world, including Pakistan. HFpEF is responsible for approximately half of all heart failure cases and is exacerbated by obesity, an escalating public health issue in Pakistan. Research has shown a high prevalence of obesity-related cardiovascular diseases amongst indigenous and immigrant Pakistani populations, with high morbidity and mortality attributable to obesity.<sup>1</sup> Although substantial advancements have been made in managing heart failure with reduced ejection fraction (HFrEF), the therapeutic options for HFpEF remain limited. While lifestyle changes and sodium-glucose cotransporter 2 (SGLT2) inhibitors have demonstrated some efficacy, there is a missing need for new pharmacological approaches.<sup>2</sup> Given the rising obesity rates in Pakistan, an innovative strategy for managing HFpEF is essential.

Tirzepatide, a new dual GIP and GLP-1 receptor agonist, has recently been shown in clinical trials to improve obesity and HFpEF outcomes. The SUMMIT trial, a randomised, placebo-controlled study, showed that tirzepatide significantly reduced the risk of cardiovascular death and worsening heart failure events in patients with HFpEF and obesity.<sup>2</sup> Patients treated with tirzepatide demonstrated a greater exercise response, improved Kansas City Cardiomyopathy Questionnaire Clinical Summary Scores, and fewer hospitalizations.<sup>3</sup> This correlates with meta-analyses that show a significant weight loss advantage with tirzepatide, which also reduces cardiovascular risks associated with obesity.<sup>4</sup> These results represent a change in paradigm toward an emphasis on metabolic intervention in cardiovascular disease.<sup>5</sup>

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Incorporating tirzepatide into Pakistan's treatment options would not only facilitate effective weight management amid the country's obesity crisis but also help mitigate one of its most costly complications—HFpEF. Addressing these two major contributors to cardiovascular disease could substantially benefit Pakistan's healthcare landscape. Given the growing burden of obesity-related heart failure and lack of access to advanced pharmacotherapy, tirzepatide could be a safe, effective, and scalable strategy. However, several challenges—such as affordability, patient adherence, and integration into existing treatment protocols—must be addressed. Policymakers in Pakistan must evaluate the feasibility of incorporating tirzepatide into national heart failure and obesity management guidelines while ensuring accessibility within the public healthcare sector. With its dual benefits in metabolic as well as cardiovascular health, tirzepatide has a potential to overhaul the treatment paradigm and improve patient outcome in Pakistan.<sup>6</sup> Its potential impact merits further exploration and policy consideration.

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