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Original Research Article

Comparative Study of Pregabalin and Sertraline in Generalized Anxiety Disorder

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Abstract:

Introduction: Anxiety, while related to fear, a complex mix of thoughts, emotions, physical sensations, and behaviors that prepare a person for situations they expect might be threatening. Key chemicals in the central nervous system that are believed to influence anxiety include norepinephrine, serotonin, dopamine, and gamma-aminobutyric acid (GABA). World Federation of Societies of Biological Psychiatry, Selective Serotonin Reuptake Inhibitors (SSRIs) like Sertraline and Selective Norepinephrine Reuptake Inhibitors (SNRIs) are considered the primary treatments for Generalized anxiety disorder (GAD). Pregabalin, an anticonvulsant, is also being used as a treatment option for GAD.

Aims & Objectives:

Aim: To compare the Efficacy, Tolerability and safety of Pregabalin (Cyclic GABA derivative) & Sertraline (Selective Serotonin Reuptake Inhibitor) in Generalized Anxiety Disorder**.**

Objectives:

Primary Objective:

1) To compare efficacy of Pregabalin and Sertraline using Hamilton Anxiety Rating scale & GAD-7 scale.

Secondary Objective:

2) To compare tolerability of Pregabalin and Sertraline.
3) Evaluating safety of Pregabalin and Sertraline using World Health Organization-Uppsala Monitoring Centre (WHO-UMC) Scale.
4) To compare both GAD-7 & Hamilton Anxiety Rating Scale [HAM-A]

Methods: A hospital based Prospective Interventional type of study was conducted in a tertiary care hospital Psychiatry department at western part of India 18 months duration from 15th April, 2024 till 6th September, 2025 in 100 Generalized Anxiety Disorder patients. GAD 7 & HAMA scale was used to evaluate the efficacy of this drug. Patients were divided into two groups. One group had received Pregabalin & other group received Sertraline. Causality of both drugs were analysed by WHO-UMC scale.

Results: 100 patients were included out of which 48 patients belonged to Pregabalin group and 52 patients belonged to Sertraline group. there were no statistically significant differences in anxiety severity between the two groups at the initiation of treatment. Over the 12-week period, both groups demonstrated a progressive reduction in mean symptom scores, reflecting an improvement in clinical condition. However, by Week 12, pregabalin was significantly more effective than sertraline in reducing symptom severity by the end of the 12-week treatment period.

Conclusion: This study demonstrated that both pregabalin and sertraline were effective in significantly reducing anxiety symptoms in patients with generalized anxiety disorder over 12 weeks. On clinician-rated HAM-A and patient-reported GAD-7, pregabalin showed modest but statistically significant superiority on week 12. Both drugs achieved substantial and comparable improvements, with pregabalin offering only a slight advantage. Also, Pregabalin showed more statistically significant outcome on HAM-A scale as compared to GAD-7 scale.

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Introduction

Fear is an instinctive response triggered by the brain when it detects immediate or looming danger, whether the threat is real or imagined. This reaction activates the body's fight-or-flight system. The word "anxiety" stems from Latin, specifically the noun angor and the verb ango, which mean "to constrict" or "to tighten." Anxiety, while related to fear, a complex mix of thoughts, emotions, physical

sensations, and behaviors that prepare a person for situations they expect might be threatening. French psychiatrist Joseph Lévy-Valensi, who lived from 1879 to 1943 and was tragically killed during the Holocaust, defined anxiété as a disturbing and dark feeling linked to anticipation. Key chemicals in the central nervous system that are believed to influence anxiety include norepinephrine, serotonin, dopamine, and gamma-aminobutyric acid (GABA). [1] The concept of generalized, ongoing, and unfocused anxiety was initially introduced by Sigmund Freud in 1894.[2]

Anxiety disorders are of different types:[3]

1) Generalized anxiety disorder
2) Panic disorder
3) Post Traumatic Stress Disorder (PTSD)
4) Separation anxiety disorder
5) Acute stress disorder
6) Phobia
7) Obsessive compulsive disorder

Anxiety disorders occur due to biological, psychological, and social factors.

Generalized anxiety disorder (GAD) is among the most prevalent mental health conditions. It involves ongoing fear, worry, and a persistent sense of being overwhelmed. GAD is marked by chronic, excessive, and unnecessary tension involving routine life matters, such as finances, family, health, or the future. This worry is typically hard to manage and is accompanied by vague psychosomatic symptoms. At the core of GAD is uncontrollable, excessive worry. [4] An estimated 4.05% of world's population has an anxiety disorder, translating to 301 million people. The number of persons affected has increased by more than 55% from 1990 to 2019. Women are 1.66 times more likely to be affected by anxiety disorders than men. [5] India has experienced rising trend, with studies indicating a rise in anxiety disorders between 23.7% and 35%. [6] In the Indian context, GAD is among the most common anxiety disorder, involving an estimated 3% to 8% of the population. [7]

Hamilton Anxiety Rating Scale [HAM-A SCALE]: earliest tools created to assess the severity of anxiety symptoms and continues to be commonly used in both clinical practice and research. It includes 14 items, each encompassing a range of symptoms, and evaluates two main components of anxiety: psychic anxiety, which refers to mental and emotional distress, and somatic anxiety, which involves physical symptoms associated with anxiety. [8][9]

Generalized Anxiety Disorder-7[GAD-7] Scale: commonly used to both identify generalized anxiety disorder and evaluate its severity. As a brief, user-friendly self-assessment tool, it allows patients to complete it quickly and independently during short outpatient visits, making it a practical option for clinicians to efficiently detect anxiety symptoms. [10]

Treatment: During 20th century, Barbiturates and meprobamate were commonly used to manage Generalized Anxiety Disorder (GAD) even though they caused high toxicity. By the 1950s, new treatment options emerged with the development of monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs).[11] Another significant class of anti-anxiety medications, benzodiazepines, also originated in the 1950s. These drugs act on the gamma-aminobutyric acid (GABA) receptors. [11] More than three decades after fluoxetine's introduction in 1986, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) continue to serve as the 1st line drug therapies for anxiety disorders. These two drug classes, both stemming from fluoxetine's development, have become standard first-line therapies.[12]

Additionally, the advent of SSRIs, SNRIs, and serotonin 5-HT1A receptor agonists like buspirone (also introduced in 1986) has significantly enhanced the medical management of anxiety. These medications are generally better tolerated and much safer in cases of overdose compared to earlier treatments.[13]

According to World Federation of Societies of Biological Psychiatry, Selective Serotonin Reuptake Inhibitors (SSRIs) and Selective Norepinephrine Reuptake Inhibitors (SNRIs) are considered the primary treatments for Generalized anxiety disorder (GAD). Pregabalin, an anticonvulsant, is also being used as a treatment option for GAD. [14]

In this study we are comparing Pregabalin with SSRI Sertraline since it is being used widely in our hospital for GAD treatment. But the pregabalin being an antiepileptic agent, there is need to explore the data on its safety, effectiveness and tolerability in GAD to make use of this medication more effectively. In this study we have chosen Sertraline as a comparator drug as it is widely available in our hospital. The present study explores the safety, efficacy and tolerability of Pregabalin in comparison with Sertraline. In this study we will also compare the two scales, HAM-A as well as GAD-7 scale. The drug Pregabalin was purchased from Pradhan Mantri Jan Aushadhi Yojana Kendra at the nearest place at lowest cost of Rs 24 for 10 tablets.

Aims & Objectives:

Aim: To compare the Efficacy, Tolerability and safety of Pregabalin (Cyclic GABA derivative) & Sertraline (Selective Serotonin Reuptake Inhibitor) in Generalized Anxiety Disorder**.**

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Secondary Objective:

2) To compare tolerability of Pregabalin and Sertraline.
3) Evaluating safety of Pregabalin and Sertraline using WHO-UMC Scale.
4) To compare both GAD-7 &Hamilton Anxiety Rating Scale [HAM-A]

Methods: This study was Prospective Interventional type of study.

Total duration of study was of 15 months.

Study Population: Generalized Anxiety Disorder patients. Study was carried out in Psychiatry department at a tertiary care hospital. Sample size: 100 patients (P-value <0.05,95% CI) Prevalence of GAD is 7% for Dahod, Gujarat.

Ethical approval: The Study Protocol, Patient information sheet and Informed consent form in Hindi, English and Gujarati languages were submitted and approved by Scientific Research Committee and Human Ethics Committee of the Institute**.**

Selection criteria: Patients who fulfilled the following criteria were taken into study: Age 18-60 years of age, Patients previously on SSRI, Insomnia Patients Both Male and Female.

Exclusion Criteria: Following patients were excluded from the study: Chronic Heart failure patients, Patients on sedatives and hypnotics, Chronic Liver failure patients, Drug Abuse patients, Chronic Kidney Disease eGFR below 60ml/min/1.73 sq.m, Pregnancy. **Study procedure:** Subjects were identified as per the inclusion and exclusion criteria. Approval of Institutional Ethics Committee was taken and Informed Consent of the patients were taken accordingly. GAD 7 & HAMA scale was used to evaluate the efficacy of this drug. Patients were divided into two groups. One group had received Pregabalin: 75 mg once daily for the first 10 days, then 75 mg twice daily from days 11 to 90. The other group had received Sertraline: 50 mg once daily for 10 days, then 100 mg once daily from days 11 to 90. HAM A and GAD-7 scores were recorded at baseline (week 0) and at weeks 1, 2, 4, 8, and 12. Causality of both drugs were analysed by WHO-UMC scale. After completion of duration of the study all the data analysis was done using descriptive statistics and a Student T test was applied to find out the probability value (<0.05) which was to be considered if this study was statistically significant.

Outcome Measures: Change in HAM-A score from Baseline to Week 12 & Change in GAD-7 score from Baseline to Week 12

Safety and Tolerability Outcomes: Adverse Events & Treatment Discontinuation Rate

Data Analysis: Data entry was done in Microsoft excel 2021.

Results & discussions: A total of 100 patients were included out of which 48 patients belonged to Pregabalin group and 52 patients belonged to Sertraline group.

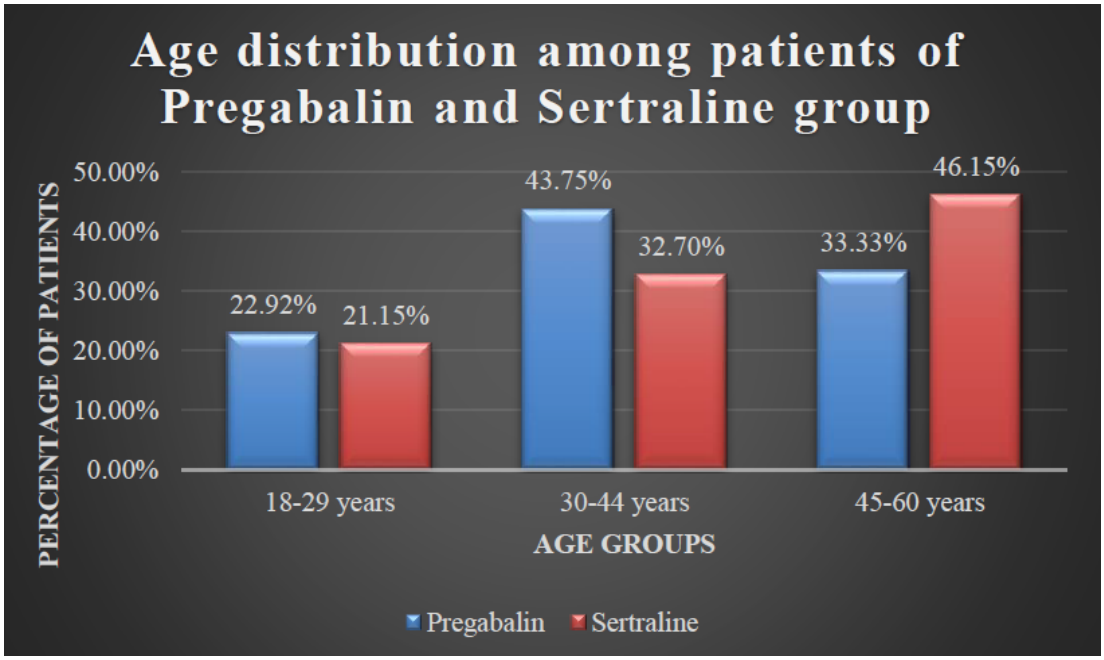

Figure 1: Age distribution of patients

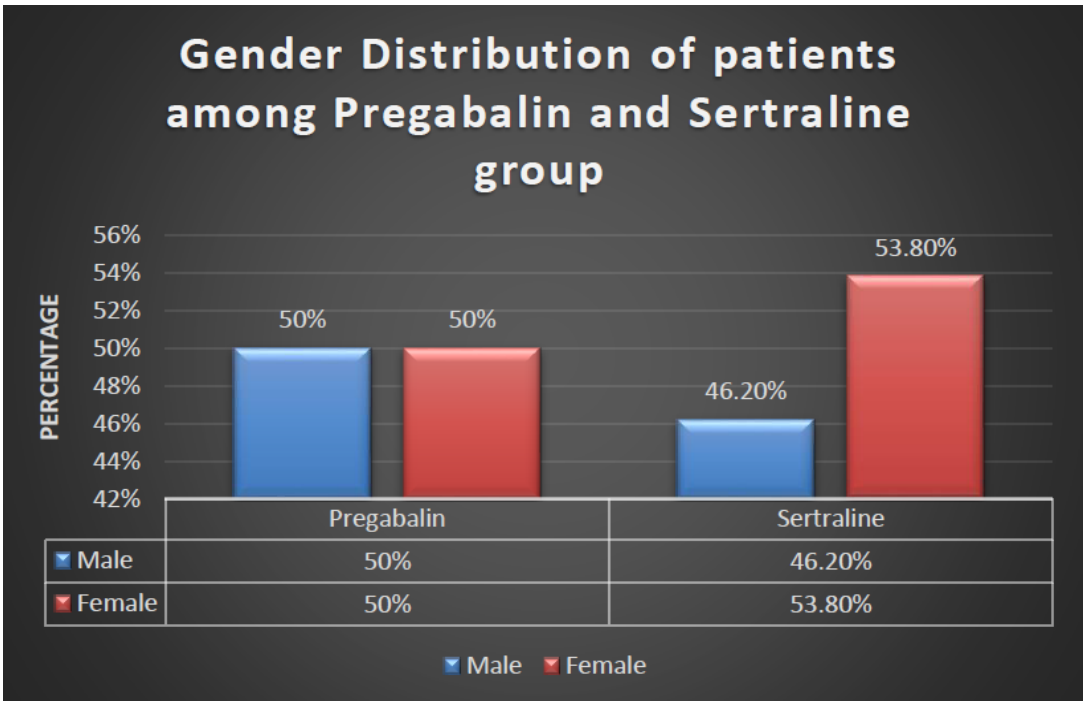

Figure 2: Gender distribution of patients

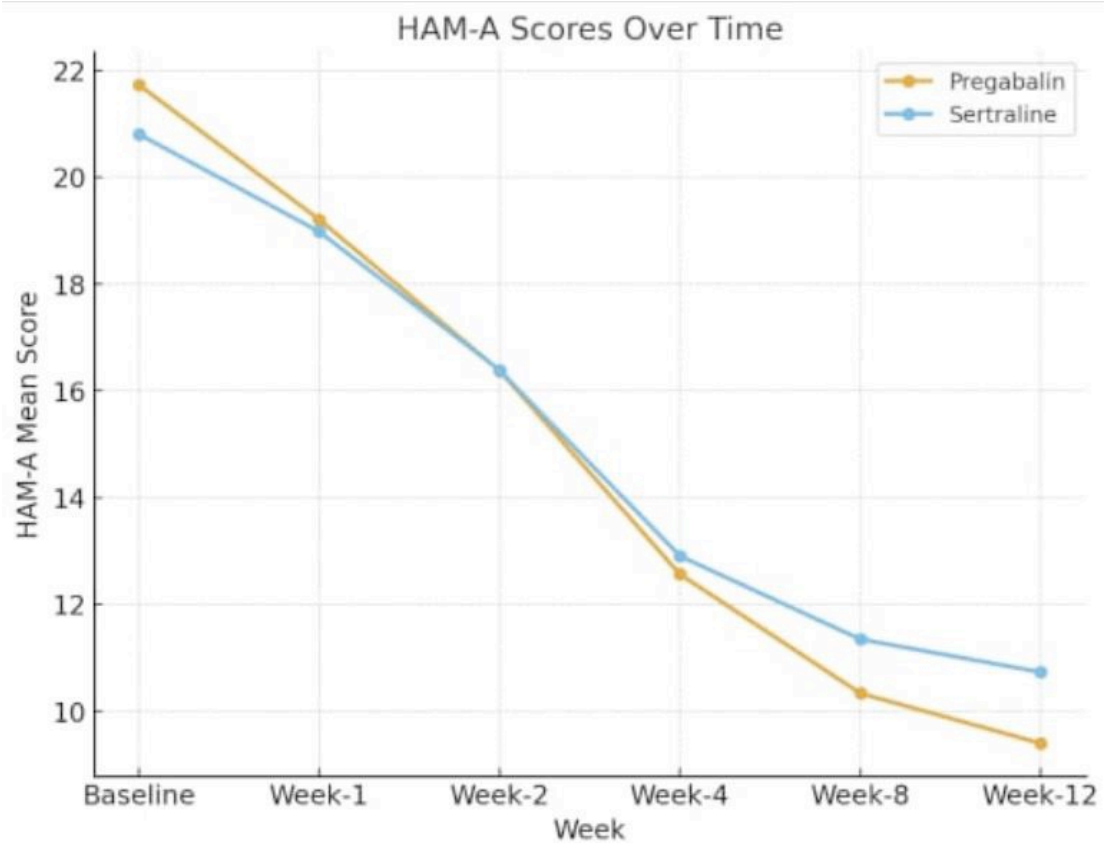

Figure 3: Change in HAM-A Scores over 12 weeks in patients receiving Pregabalin versus Sertraline

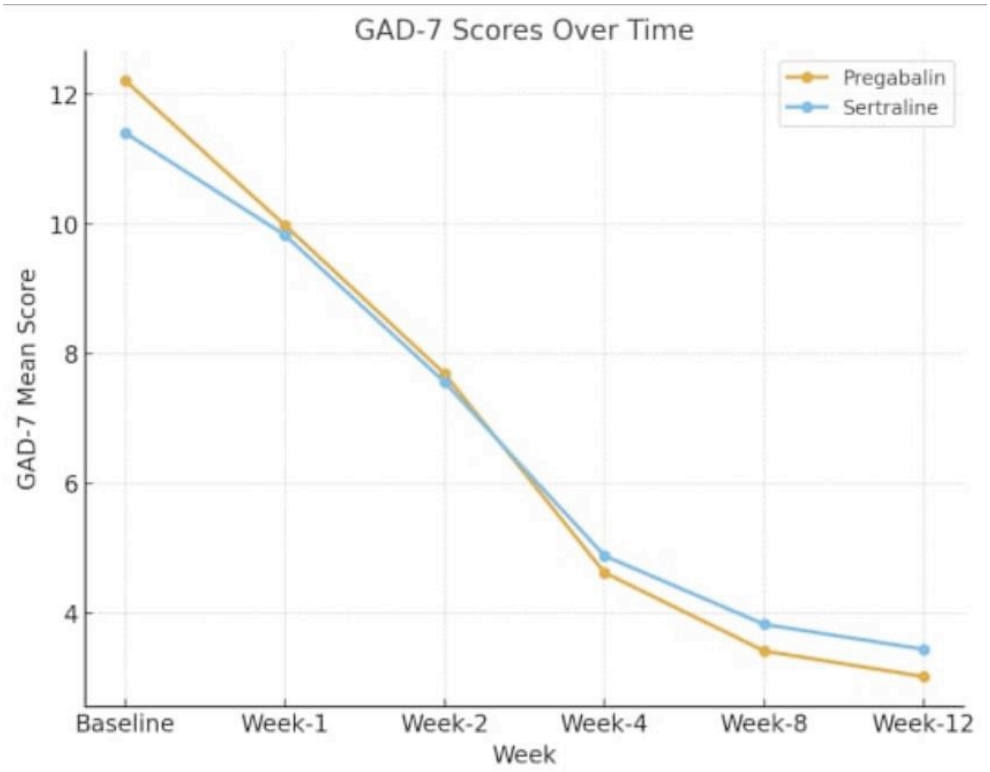

Figure 4: Change in GAD-7 Scores over 12 weeks in patients receiving Pregabalin versus Sertraline

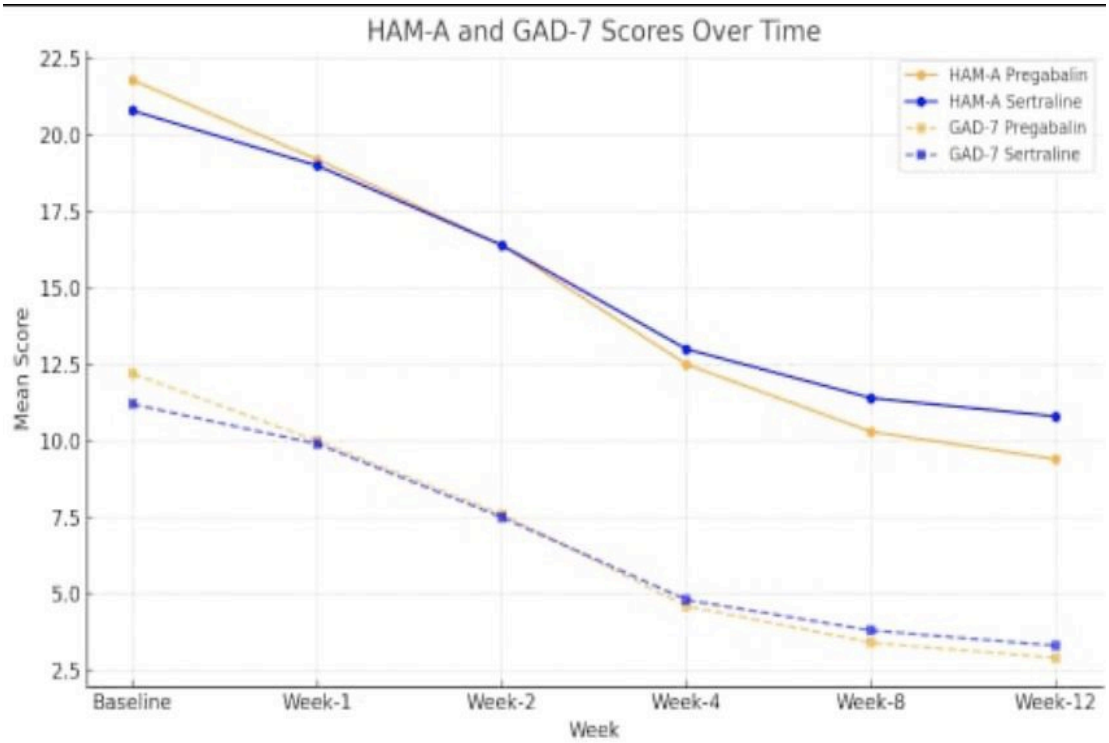

Figure 6: Comparison of Clinician Rated (HAM-A) Scale and Patient Rated (GAD-7) Scale Anxiety Outcomes over 12 weeks

Overall Trends and Group Comparisons: In the current study, anxiety symptom severity was assessed using both the Hamilton Anxiety Rating Scale (HAM-A) and the Generalized Anxiety Disorder 7-item (GAD-7) scale across multiple time points in two treatment groups: Pregabalin and Sertraline. A comparative analysis of these two scales was performed to evaluate their sensitivity to

change over time and to determine any significant differences in treatment efficacy between the groups. Both HAM-A and GAD-7 scores demonstrated a progressive reduction over the 12-week treatment period in both groups, indicating an overall improvement in anxiety symptoms.

At baseline, the mean HAM-A scores were 21.73 ± 4.21 for the Pregabalin group and 20.81 ± 3.01 for the Sertraline group ($p = 0.21$), while the mean GAD-7 scores were 12.21 ± 2.81 and 11.40 ± 2.70, respectively ($p = 0.15$). These results suggest that there were no statistically significant differences in anxiety severity between the two groups at the initiation of treatment.

Throughout the course of the study, both treatment arms showed a gradual decline in scores on both scales. However, statistically significant differences between the groups emerged only at Week 12. On the HAM-A scale, the Pregabalin group showed significantly lower anxiety scores compared to the Sertraline group (mean difference = -1.53, $p = 0.038$). Similarly, on the GAD-7 scale, a significant difference was observed in favor of Pregabalin at Week 12 (mean difference = -0.92, $p = 0.046$).

Comparison of HAM-A and GAD-7 Scales: While both scales were effective in detecting symptom improvement over time, several distinctions can be noted. The HAM-A is a clinician-rated instrument that encompasses a broad range of anxiety symptoms, including both psychological and somatic domains. Its wider scoring range (0–56) allows for a more granular assessment of symptom severity. In contrast, the GAD-7 is a self-reported scale specifically designed to screen for and assess generalized anxiety disorder, with a narrower scoring range (0–21).

In the current analysis, both scales demonstrated comparable sensitivity in detecting treatment effects, as evidenced by the statistically significant differences observed at the endpoint (Week 12). However, the HAM-A showed a slightly larger absolute difference in mean scores between the groups, possibly due to its more comprehensive nature and broader scoring range. Notably, both instruments failed to detect any significant differences between groups at earlier time points, suggesting similar performance in the early stages of treatment.

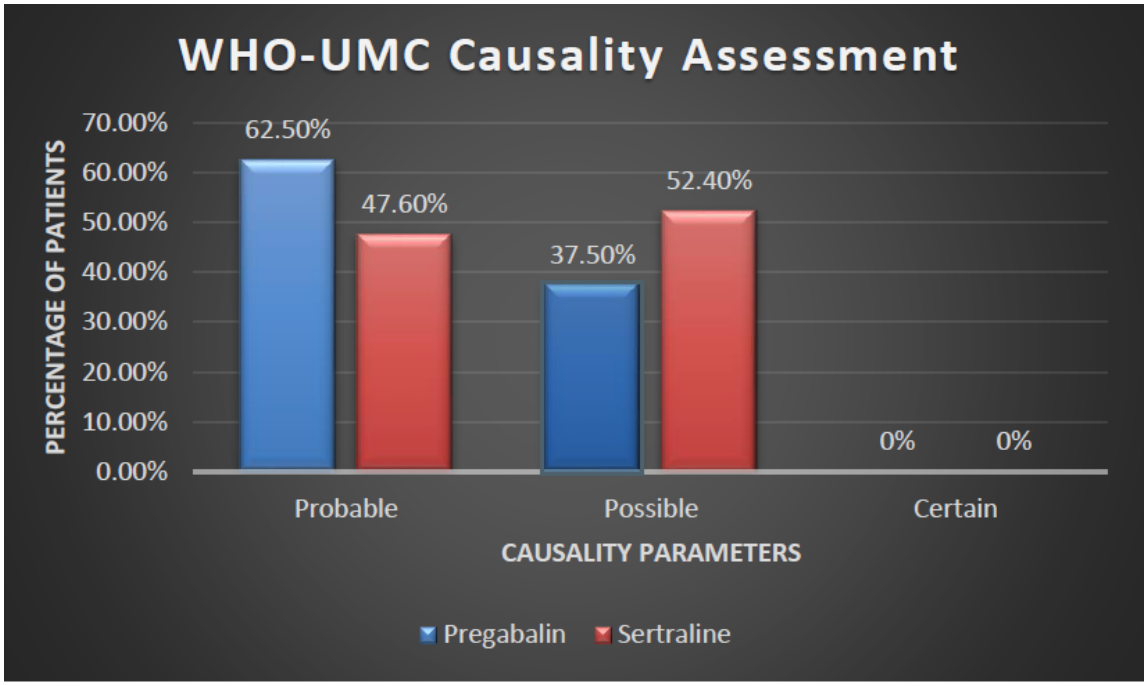

Figure 7: WHO-UMC Causality Assessment for Pregabalin and Sertraline groups:

The causality assessment of adverse drug reactions (ADRs) was conducted using the WHO-UMC system for both Pregabalin and Sertraline. Among the 16 ADR cases attributed to Pregabalin, 62.5% (n=10) were classified as Probable, and 37.5% (n=6) as Possible, with no cases rated as Certain. Similarly, for Sertraline, out of 21 ADR cases, 47.6% (n=10) were deemed Probable, and 52.4% (n=11) as Possible, also with no Certain causality recorded.

A Chi-square test was performed to assess whether the distribution of causality categories differed significantly between the two drugs. The resulting P-value was 0.37, indicating no statistically significant difference in the causality assessment distribution between Pregabalin and Sertraline ($P > 0.05$).

Conclusion:

This study demonstrated that both pregabalin and sertraline were effective in significantly reducing anxiety symptoms in diabetic patients with generalized anxiety disorder over 12 weeks.

On clinician-rated HAM-A and patient-reported GAD-7, pregabalin showed modest but statistically significant superiority on week 12. Both drugs achieved substantial and comparable improvements, with pregabalin offering only a slight advantage. Also, Pregabalin showed more statistically significant outcome on HAM-A scale as compared to GAD-7 scale.

Taken together, these findings suggest that while both scales captured meaningful reductions, the HAM-A scale proved more sensitive in differentiating between treatments, particularly for clinician-observed somatic anxiety symptoms.

Both treatments were well tolerated, with adverse drug reactions being mild to moderate in nature and not leading to treatment discontinuation. Pregabalin was more commonly associated with somnolence and dizziness, while sertraline produced gastrointestinal and sleep-related effects, reflecting their known pharmacological profiles.

Overall, the findings confirm that pregabalin and sertraline are both safe and effective for managing anxiety symptoms. But Pregabalin may offer advantages in terms of faster onset and modestly greater efficacy in later weeks.

Limitation of the study:

- Sample size and single-center design: The relatively modest sample of 100 patients, all recruited from a single center, limits the generalizability of the findings to broader populations.
- Absence of placebo control: Without a placebo arm, it is not possible to fully disentangle treatment-related improvements from nonspecific factors such as expectancy or natural course of illness.
- Short duration of follow-up: The study was limited to 12 weeks; therefore, long-term efficacy and safety beyond this period remain unknown.
- Open-label nature: If the study was not blinded, risk of observer and reporting bias could have influenced clinician-rated and patient-reported outcomes.

References:

1. Chand SP, Marwaha R. Anxiety [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan– [updated 2023 Apr 24; cited 2025 Oct 6]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470361/
2. Rickels K, Rynn MA. What is generalized anxiety disorder? J Clin Psychiatry. 2001;62 Suppl 11:4–12; discussion 13–4. PMID: 11414550.: https://pubmed.ncbi.nlm.nih.gov/11414550/
3. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's: The pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill Education; 2017.
4. Munir S, Takov V. Generalized Anxiety Disorder [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan– [updated 2022 Oct 17; cited 2025 Oct 6]. Available from: https://pubmed.ncbi.nlm.nih.gov/28722900/
5. Javaid SF, Hashim IJ, Hashim MJ, et al. Epidemiology of anxiety disorders: global burden and sociodemographic associations. Middle East Curr Psychiatry. 2023; 30:44. doi: 10.1186/s43045-023-00315-3. https://doi.org/10.1186/s43045-023-00315-3
6. Szuhany KL, Simon NM. Anxiety disorders: a review. JAMA. 2022 Dec 27;328(24):2431–45. doi: 10.1001/jama.2022.22744. https://pubmed.ncbi.nlm.nih.gov/36573969/
7. Shivalkar R, Sengupta S. Anxiety disorders. Natl Med J India. 2023; 36:241–5. doi: 10.25259/NMJI_530_2022. https://nmji.in/anxiety-disorders/
8. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol. 1959; 32:50–55. https://dcf.psychiatry.ufl.edu/files/2011/05/HAMILTON-ANXIETY.pdf
9. Maier W, Buller R, Philipp M, Heuser I. The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. J Affect Disord. 1988;14(1):61–8. https://pubmed.ncbi.nlm.nih.gov/2963053/
10. Li M-Y, Lan L. Characteristics of commonly used anxiety and depression scales and their rational application in general hospitals. Psychosomatic Gastroenterology (PG). 2019 Jun 20. http://www.pgonline.net/Articles/detail/id/304
11. Votaw VR, Geyer R, Rieselbach MM, et al. The epidemiology of benzodiazepine misuse: a systematic review. Drug Alcohol Depend. 2019; 200:95–114. doi: 10.1016/j.drugalcdep.2019.02.033. https://www.sciencedirect.com/science/article/abs/pii/S0376871619301425?via%3Dihub
12. Benfield P, Heel RC, Lewis SP. Fluoxetine: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in depressive illness. Drugs. 1986; 32:481–508. doi: 10.2165/00003495-198632060-00002.

https://doi.org/10.2165/00003495-198632060-00002

13. Bui E, King F, Melaragno A. Pharmacotherapy of anxiety disorders in the 21st century: a call for novel approaches. Gen Psychiatr. 2019 Dec 11;32(6): e100136. doi: 10.1136/gpsych-2019-100136. https://pmc.ncbi.nlm.nih.gov/articles/PMC6936967/
14. Cvjetkovic-Bosnjak M, Soldatovic-Stajic B, Babovic SS, Boskovic K, Jovicevic M. Pregabalin versus sertraline in generalized anxiety disorder: an open label study. Eur Rev Med Pharmacol Sci. 2015;19(11):2120–4. Available from: https://www.europeanreview.org/wp/wp-content/uploads/2120-2124.pdf