Original Article

Comparative Analysis of Escitalopram, Sertraline and Amitriptyline in Patients with Major Depressive Disorder in India : A Real-World Study

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Abstract

Background and Objective : Major Depressive Disorder (MDD) is one of the leading causes of non-fatal disease burden in India. Researchers have been trying to find the best therapy for Depression for many years. Limited data on antidepressants in clinical practice highlights the need for more real-world evidence. This study aimed to compare the efficacy and safety of Escitalopram, Sertraline and Amitriptyline in patients with MDD.

Materials and Methods : This was a real-world, observational, prospective study conducted in India between May, 2021 and April, 2023.

Results : Overall, 268 patients were enrolled in the study (Escitalopram [n=101]; Sertraline [n=87]; Amitriptyline [n=80]). While a reduction in Hamilton Depression Rating Scale-17 (HAM-D 17) scores was reported over time in each cohort, the change in HAM-D 17 scores from baseline for Escitalopram was significantly higher than Sertraline ($p<0.005$) and Amitriptyline ($p<0.005$), with no significant difference between Sertraline and Amitriptyline. At Week 8, Clinical Global Impression, European Quality of Life Five Dimension Five Level-health states, and visual analogue scale values in the Escitalopram cohort were significantly lower than Sertraline ($p<0.005$ each) and Amitriptyline cohorts ($p<0.005$ each). Columbia-Suicide Severity Rating Scale scores were also significantly lower in the Escitalopram cohort compared to Sertraline ($p=0.01$) and Amitriptyline ($p=0.002$). Adverse events were reported by 245 (91.4%) patients during the study. Insomnia (42.6%), Nausea (31.0%) and Constipation (81.3%) were most frequent in Escitalopram, Sertraline and Amitriptyline cohorts, respectively.

Conclusion : Escitalopram elicited better responses and significantly improved Quality of Life compared to Sertraline and Amitriptyline. No new safety concerns were observed.

Key words : Amitriptyline, Antidepressants, Escitalopram, India, Real-world, Sertraline.

Mental health issues are a significant cause of non-fatal disease burden in India, with their proportional contribution nearly doubling since 1990. Major Depressive Disorder (MDD), characterized by persistent low mood, loss of interest in pleasurable activities, guilt, lack of energy, concentration difficulties, appetite changes, sleep disturbances and suicidal thoughts, is a prevalent condition. In 2019, the prevalence of MDD in the Indian population was 2.68%, with higher prevalence in the 40-59 years age group[1].

MDD can be managed with various treatment modalities. Per Indian Psychiatric Society (IPS) guidelines, treatment begins with thorough patient assessment and typically involves medication and/or psychotherapy. While some antidepressants show higher response rates in clinical trials, ongoing debate surrounds their efficacy and safety. Many patients experience only partial relief or relapse within weeks of treatment[2]. However, data on inadequate response and relapse rates in the Indian population is limited. In India, selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed medicines for Depression[3], followed by Tricyclic Antidepressants (TCAs)[4]. Despite their known Adverse Events (AEs), antidepressants are frequently prescribed. Escitalopram, despite causing more AEs and sexual disturbances compared to other antidepressants[5], is the preferred monotherapy in >65% of patients[6]. Similarly, other commonly prescribed antidepressants like Sertraline and Fluoxetine also elicit multiple AEs[7]. Some antidepressants, like Escitalopram and Sertraline, have also been reported to induce suicidal ideation[8], although conclusive data on this topic is limited[9].

Antidepressant use is considerable, especially in the Western World, and increasing in several countries[10].

Editor's Comment :

- Escitalopram was found to elicit a significant reduction in HAM-D 17, CGI-S, and CGI-I scores, help achieve response in higher number of patients (97% *versus* 67.8% *versus* 73.8%), and significantly improve the QoL compared to Sertraline ($p<0.005$) and Amitriptyline ($p<0.005$) at Week 8 in this real-world study.
- All three antidepressants reduced suicidal tendency (C-SSRS scores), with significantly better results observed in the Escitalopram cohort ($p=0.004$).
- The adverse events observed during the study were consistent with the known safety profile of the drugs; 95%, 82.8%, and 96.2% of patients had AEs in the Escitalopram, Sertraline, and Amitriptyline cohorts, respectively.

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Globally, both Psychotherapy and Pharmacotherapy have demonstrated efficacy in alleviating patients' symptoms and Quality of Life (QoL)[11]. However, in India, the prescription patterns for antidepressants have known to deviate from the World Health Organization (WHO) recommendations[12], with reported off-label use, high dropout rate from clinical trials, and poor adherence to medications[12]. The limited research on the overall efficacy and safety of antidepressants in India[13] indicates the need for more real-world evidence.

This real-world study aimed to compare the efficacy and safety of three antidepressants, Escitalopram, Sertraline, and Amitriptyline, in patients with MDD in India. It also assessed their impact on the QoL and suicidal risk.

Materials and Methods

Study Design :

This real-world, observational, comparative, prospective study was conducted at the Department of Psychiatry, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai, Maharashtra, India, between May, 2021 and April, 2023. Patients were followed-up for 8 weeks. The study protocol was approved by the Institutional Ethics Committee of Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai (Registration number: ECR/ 266/ Lokmanya/ Inst/ MH/ 2013RR 16; Study approval number: IEC/40/21). The study was conducted in accordance with Good Clinical Practice and the ethical principles outlined in the Declaration of Helsinki 2008. Informed consent was obtained from patients or parents/ legal guardians for children under the age of 18.

Study Population :

Patients of all age groups were eligible to be enrolled into the study if they presented episode(s) of MDD (diagnosed by psychiatrist), had Hamilton Depression Rating Scale-17 (HAM-D 17) total score of $\geq$15 or a Clinical Global Impression-Severity of illness (CGI-S) score of $\geq$3, and were prescribed either of the three study drugs by the treating Psychiatrist (based on age, disease severity, comorbid conditions etc). Patients with current or a history of seizure disorder, bipolar disorder, schizophrenia, or brain injury were excluded from the study.

Study Therapy :

The three study drugs Escitalopram, Sertraline, and Amitriptyline were prescribed by the Psychiatrist per standard practice. Although the typical starting dose for Escitalopram, Sertraline, and Amitriptyline is 10 mg[14], 50 mg[15], and 25 mg[16] per day, respectively, the dose for this study was determined by the treating psychiatrist based on the disease severity, age, comorbidities, etc. Dose adjustments were allowed at any time during the study. Patients were allowed to continue medication for general illnesses such as Diabetes or Hypertension. All assessments were performed every 2 weeks until Week 8.

Data Collection :

Baseline demographic and clinical details were collected at Visit 1. Subsequent data were collected during the routine patient visits at Week 2, Week 4, Week 6 and Week 8. Data were collected by the psychiatrists on a predefined case report form (CRF). Patients were divided into three groups based on the prescribed antidepressant.

Efficacy Assessment :

Scores from the various assessment tools (Total HAM-D 17, HAM-D 17 subscores, CGI-S, CGI Scale-Global Improvement [CGI-I], European Quality of Life Five Dimension Five Level [EQ-5D-5L], and Columbia-Suicide Severity Rating Scale [C-SSRS]) were recorded on the CRF at each visit. The primary endpoint of the study was the change in HAM-D 17 scores from baseline up to Week 8 between and within therapies. Secondary endpoints included response and remission rates, change in HAM-D 17 subscale scores, change in CGI-S and CGI-I scores, and QoL scores over time. Response was defined as a decrease in HAM-D 17 total score at Week 8 relative to baseline by $\geq$50%. Remission was defined as HAM-D 17 total score of $\leq$7 at Week 8. The QoL was assessed by the EQ-5D-5L scale.

Safety Assessment :

AEs (including grade/severity) and C-SSRS scores for suicidal ideation/behaviour were monitored during each visit.

Statistical Analysis :

Statistical Package for the Social Sciences (SPSS) version 26.0 was used for analyses. The data were analyzed using non-parametric tests as the data did not follow a normal distribution. Kolmogorov-Smirnov tests were performed on the actual data ($p<0.05$ for each cohort), percent change from baseline data ($p<0.05$ for each cohort), and log-transformed data ($p<0.05$ for each cohort). However, it did not satisfy the assumptions of normality. The Kruskal-Wallis test was used for overall comparison between the three cohorts, and the Wilcoxon signed-rank test for pairwise comparisons. All the tests were two-tailed, with a significance level (α) of 0.05.

Results

Among 268 patients included in the analyses, 101 patients received Escitalopram, 87 received Sertraline, and 80 received Amitriptyline. There were 54.5%, 57.5% and 61.3% of men, and the mean (SD) age of patients was 41.8 (13.8) years, 35.5 (13.1) years, and 39.3 (11.8) years, in the three cohorts, respectively. At baseline, the mean doses of the antidepressants were 9.6 (±4.1) mg, 33.5

(±12.1) mg, and 30.3 (±11.5) mg, respectively. There were no significant differences between the HAM-D 17, CGI-S, total EQ-5D-5L health state values, VAS, or C-SSRS scores in the three cohorts at baseline (Table 1).

Efficacy Evaluation :

Hamilton Depression Rating Scale-17 (HAM-D 17)

The change in HAM-D 17 scores from baseline to each time point was compared among the three cohorts. A significant difference was observed between the three cohorts at each timepoint (Table 2, Fig 1A). The change in HAM-D 17 scores from baseline for the Escitalopram cohort was significantly higher than the Sertraline ($p<0.005$) and Amitriptyline cohorts ($p<0.005$), with no significant difference observed between the latter two.

Each cohort was also analyzed separately. A significant reduction ($p<0.005$) in HAM-D 17 scores was reported at Week 2, Week 4, Week 6, and Week 8 compared to baseline for each cohort (Table 2).

Response and Remission Rates

Overall, response was achieved by <20% of patients at Week 2 and increased gradually. In all three cohorts, >60% of patients achieved response at Week 8. The response rate was higher in the Escitalopram than the Sertraline and Amitriptyline cohorts at all the study time points (Fig 1B)

Remission was achieved by <10% of patients at Week 2 across all three cohorts and increased gradually thereafter. However, >50% of patients on Escitalopram achieved remission at Week 4, and >72.3% at Week 8, while the rate of remission stayed <40% at Week 8 for Sertraline and Amitriptyline cohorts (Fig 1C).

Table 1 — *Baseline demographic and clinical characteristics of patients*

	Escitalopram (n=101)	Sertraline (n=87)	Amitriptyline (n=80)	*p*-value
Age (years), mean (SD)	41.8 (13.8)	35.5 (13.1)	39.3 (11.8)	0.002
Sex				0.656
Male, n (%)	55 (54.5)	50 (57.5)	49 (61.3)	NA
Female, n (%)	46 (45.5)	37 (42.5)	31 (38.8)	NA
Concomitant medication, n (%)	20 (19.8)	16 (18.4)	22 (27.5)	0.308
Dose (mg), mean (SD)	9.6 (4.1)	33.5 (12.1)	30.3 (11.5)	NA
HAM-D 17 score, mean (SD)	24.8 (8.4)	25.9 (6.5)	24.0 (6.5)	0.531
CGI-S score, mean (SD)	5.2 (1.1)	4.7 (1.2)	4.3 (0.9)	0.066
EQ-5D-5L health state value score, mean (SD)	14.4 (3.5)	14.4 (4.0)	13.1 (3.1)	0.824
Mobility	1.7 (0.9)	2.4 (1.0)	2.2 (0.9)	NA
Self-care	2.2 (1.1)	2.7 (1.0)	2.1 (0.9)	NA
Pain	2.9 (1.2)	2.7 (1.2)	3.1 (0.9)	NA
Anxiety/depression	4.1 (0.9)	3.4 (1.0)	3.2 (0.6)	NA
Usual activities	3.4 (1.0)	3.2 (0.9)	2.6 (0.8)	NA
EQ-5D-5L visual analogue score, mean (SD)	74.2 (16.3)	67.2 (18.4)	59.0 (16.1)	0.069
C-SSRS score, mean (SD)	2.1 (2.5)	1.7 (2.3)	1.8 (2.8)	0.239
Patients with suicidal tendency/ideation, n (%)	59 (58.4)	49 (56.3)	45 (56.3)	0.944

CGI-S:Clinical Global Impression-Severity of illness, C-SSRS:Columbia-Suicide Severity Rating Scale, EQ-5D-5L:European Quality of Life Five Dimension Five Level, HAM-D 17:Hamilton Depression Rating Scale-17, SD:Standard Deviation.

HAM-D 17 Subscale Scores

To better understand the efficacy of antidepressants, few components of HAM-D 17 were compared between the groups at Week 8 (Table 2). The scores for Escitalopram cohort were significantly lower than Sertraline ($p<0.005$) and Amitriptyline ($p<0.005$) on most subscales (depressed mood, sleep disorder, work and activities, anxiety, somatic symptoms, hypochondriasis, and insight). For the retardation subscale, both Escitalopram ($p<0.005$) and Amitriptyline cohort ($p=0.006$) had significantly lower scores than Sertraline. For hypochondriasis, the scores for Sertraline were significantly lower than Amitriptyline cohort ($p=0.023$).

Clinical Global Impression (CGI)

The CGI-S values for all three cohorts reduced over time. A significant difference was observed between CGI-S scores of the three cohorts at Week 2 ($p=0.001$), Week 6 ($p=0.002$), and Week 8 ($p<0.005$). At Week 8, patients in the Escitalopram cohort had significantly lower scores ($p<0.005$) than the other two cohorts, while the scores of Sertraline and Amitriptyline cohorts were not statistically different from each other (Fig 2A).

The CGI-I values for all three cohorts reduced over time. The CGI-I values in the Escitalopram cohort were significantly lower at Week 6 and Week 8 compared to the Sertraline ($p<0.005$) and Amitriptyline cohorts ($p<0.005$) (Fig 2B).

EQ-5D-5L Health State Values and Visual Analogue Scale (VAS)

At Week 8, the total EQ-5D-5L values and individual values for all 5 dimensions in the Escitalopram cohort were significantly lower than Sertraline ($p<0.005$) and Amitriptyline cohorts ($p<0.005$) (Table 2). At Week 8, total EQ-5D-5L values for Sertraline and Amitriptyline cohorts were not statistically different from each other, and for the dimensions of mobility, anxiety, and usual activities. For the dimension of self-care, Amitriptyline cohort reported significantly lower values than Sertraline ($p=0.022$), and for pain, Sertraline cohort had significantly lower values ($p=0.013$) compared to Amitriptyline (data not shown).

The VAS scores for all 3 cohorts reduced over time (Fig 2C). A significant difference was observed between the three cohorts at Week 2 ($p<0.005$), Week 4 ($p=0.027$), Week 6 ($p=0.003$), and Week 8 ($p<0.005$). While patients in the Amitriptyline cohort had significantly lower VAS scores compared to the other two cohorts ($p<0.005$) at Week 2, patients in the Escitalopram cohort reported significantly lower values ($p<0.005$) at Week 8. Sertraline and Amitriptyline cohorts did not report statistically different values at Week 8.

Table 2 — *Comparison of change in HAM-D 17 scores between and within cohorts at each time point, and summary of HAM-D 17 subscale scores, EQ-5D-5L health state values, and C-SSRS scores*

Change in HAM-D 17 scores between cohorts

	Escitalopram (n=101)	Sertraline (n=87)	Amitriptyline (n=80)			Escitalopram vs Sertraline	Escitalopram vs Amitriptyline	Sertraline vs Amitriptyline
	Change in HAM-D 17 score			H*	p-value	p-value (pair-wise comparisons)		
Change from Baseline to Week 2	7 (4-10)	3 (3-5)	3 (2-4)	55.6	<0.005	<0.005	<0.005	0.691
Change from Baseline to Week 4	13 (9-20)	7 (6-11)	7 (6-9)	54.2	<0.005	<0.005	<0.005	0.200
Change from Baseline to Week 6	16 (13-23)	11 (9-14.5)	11 (8-13.25)	48.1	<0.005	<0.005	<0.005	0.223
Change from Baseline to Week 8	18 (15-25)	15 (12-18)	15 (11.75-17)	36.7	<0.005	<0.005	<0.005	0.236

Change in HAM-D 17 scores within cohorts

	Escitalopram (n=101)		Sertraline (n=87)		Amitriptyline (n=80)	
	HAM-D 17 score	p-value	HAM-D 17 score	p-value	HAM-D 17 score	p-value
Baseline	26 (18-30)	NA	24 (22-28)	NA	25 (18-28)	NA
Week 2	17 (12-24)	<0.005	21 (18-24)	<0.005	22 (15-24.25)	<0.005
Week 4	7 (5-16)	<0.005	17 (12-20)	<0.005	17.5 (11-20)	<0.005
Week 6	4 (2-12)	<0.005	14 (7-16.5)	<0.005	14 (6-17)	<0.005
Week 8	1 (0-8)	<0.005	11 (4-13)	<0.005	10 (3.75-14)	<0.005

HAM-D 17 subscale scores at Week 8

	Escitalopram (n=101)	Sertraline (n=87)	Amitriptyline (n=80)		Escitalopram vs Sertraline	Escitalopram vs Amitriptyline	Sertraline vs Amitriptyline
	Subscale score			p-value	p-value (pair-wise comparisons)		
HAM-D 17 depressed mood subscale	0 (0-1)	1 (1-1)	1 (1-1.25)	<0.005	<0.005	<0.005	0.365
HAM-D 17 sleep disorder subscale	0 (0-0)	0 (0-1)	0 (0-1)	<0.005	<0.005	<0.005	0.756
HAM-D 17 work and activities subscale	0 (0-0)	1 (0-1)	0 (0-2)	<0.005	<0.005	<0.005	0.712
HAM-D 17 retardation subscale	0 (0-0)	0 (0-1)	0 (0-0)	0.001	<0.005	0.430	0.006
HAM-D 17 anxiety somatic symptoms subscale	0 (0-0)	1 (0-1)	1 (0-1)	<0.005	<0.005	<0.005	0.550
HAM-D 17 hypochondriasis subscale	0 (0-0)	0 (0-0)	0 (0-1)	<0.005	0.005	<0.005	0.023
HAM-D 17 insight subscale	0 (0-0)	0 (0-1)	0 (0-1)	0.001	0.021	<0.005	0.201

EQ-5D-5L health state values

	Escitalopram (n=101)	Sertraline (n=87)	Amitriptyline (n=80)		Escitalopram vs Sertraline	Escitalopram vs Amitriptyline	Sertraline vs Amitriptyline
	Health state value score (Total score)			p-value	p-value (pair-wise comparisons)		
Baseline	14 (11-16)	13 (12-16)	14 (12-16)	0.824	NA	NA	NA
Week 2	11 (10-13)	11 (9-14)	11(9-13)	0.428	NA	NA	NA
Week 4	8 (7-10)	9 (8-11)	10 (8-11)	<0.005	<0.005	<0.005	0.733
Week 6	6 (6-7)	8 (7-9)	8 (6-10)	<0.005	<0.005	<0.005	0.715
Week 8	5 (5-6)	7 (6-8)	7(6-8)	<0.005	<0.005	<0.005	0.642

C-SSRS scores

	Escitalopram (n=101)	Sertraline (n=87)	Amitriptyline (n=80)		Escitalopram vs Sertraline	Escitalopram vs Amitriptyline	Sertraline vs Amitriptyline
	CSSRS score			p-value	p-value (pair-wise comparisons)		
Baseline	2 (0-3)	1 (0-2)	1 (0-2)	0.240	NA	NA	NA
Week 2	0 (0-2)	0 (0-2)	0 (0-1)	0.216	NA	NA	NA
Week 4	0 (0-0)	0 (0-0)	0 (0-0)	0.710	NA	NA	NA
Week 6	0 (0-0)	0 (0-0)	0 (0-0)	0.005	0.004	0.008	0.875
Week 8	0 (0-0)	0 (0-0)	0 (0-0)	0.004	0.010	0.002	0.614

*The test statistic is adjusted for ties. All values are presented as median and interquartile range. C-SSRS, Columbia-Suicide Severity Rating Scale; EQ-5D-5L, European Quality of Life Five Dimension Five Level; H, Kruskal Wallis H statistic; HAM-D 17, Hamilton Depression Rating Scale-17.

Safety Evaluation :

Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS scores were not significantly different between the three cohorts at baseline, Week 2 and Week 4, but reduced over time (Table 2). At Week 6 and Week 8, the scores were significantly lower in Escitalopram compared to Sertraline (p=0.004; p=0.01) and Amitriptyline cohorts (p=0.008; p=0.002).

Similarly, there was a reduction in the number of patients with suicidal ideation/behaviour over time in all three cohorts (Fig 3).

Adverse Events (AEs)

During the study, AEs were reported by 245 (91.4%) patients: Escitalopram: 96 (95%), Sertraline: 72 (82.8%), and Amitriptyline: 77 (96.2%). The most frequently reported AEs were insomnia (42.6%) and nausea (35.6%) with Escitalopram, nausea (31.0%) and anorexia (29.9%) with Sertraline, and constipation (81.3%) and dry mouth (61.3%) with Amitriptyline. Most were Grade 1 or Grade 2 in intensity. Table 3 summarizes the AEs reported during the study. In addition to the solicited AEs listed in the CRF, two unsolicited AEs of irritability (n=1) and erectile dysfunction (n=2) were reported.

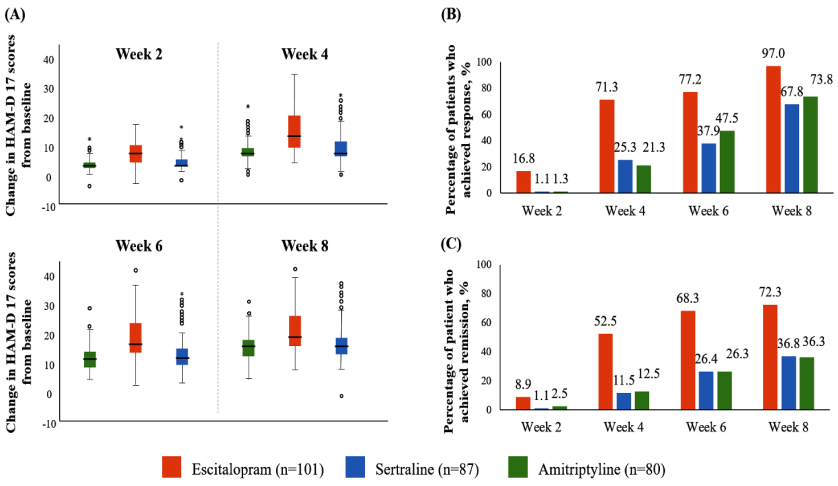

Fig 1 — (A) Comparison of change in HAM-D 17 scores between cohorts at each time point, (B) Response rates from baseline to Week 8, and (C) Remission rates from baseline to Week 8

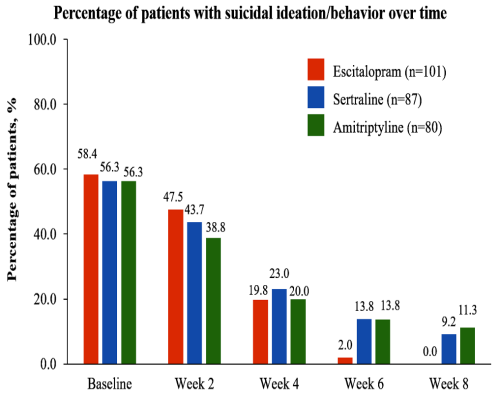

Fig 3 — Percentage of patients with suicidal ideation/ behavior over time

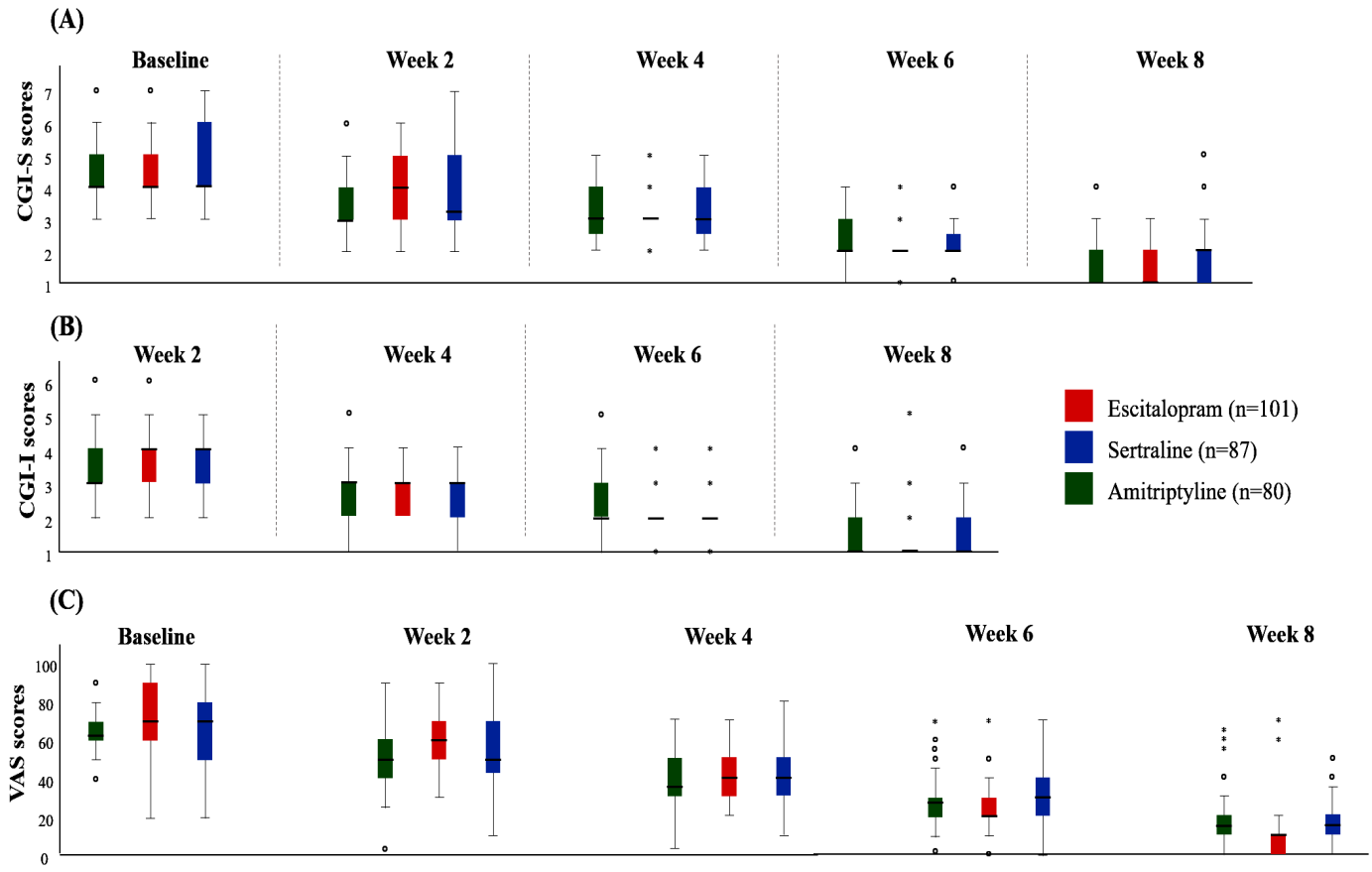

Fig 2 — (A) Comparison of CGI-S, (B) CGI-I, and (C) EQ-5D-5L-VAS scores between cohorts at each time point

Discussion

To the best of our knowledge, this is the first study comparing the efficacy and safety of three commonly prescribed antidepressants, Escitalopram, Sertraline, and Amitriptyline, in the real-world in the Indian population. The HAM-D 17 is widely recognised for its reliability in measuring depression[17]. Depression is associated with substantial disability[18], underscoring the importance of investigating the potential impact of antidepressants on QoL. Data of the first 50 patients has been previously published[2].

Previously, global and Indian studies have demonstrated improvement with Escitalopram[19] and Sertraline[7]. By Week 2, all three antidepressants led to a significant decrease in HAM-D 17 scores, consistent with existing literature indicating early onset of action compared to placebo[7,20]. Escitalopram was found to be better than Sertraline and Amitriptyline, exhibiting significantly lower HAM-D 17, CGI-S, and CGI-I scores. Escitalopram has previously demonstrated comparable efficacy to Agomelatine, Desvenlafaxine[21] and Duloxetine in the Indian population, with early onset[22] and statistically better efficacy than Desvenlafaxine[23]. In this study, Escitalopram continued to show significantly higher overall efficacy and superiority in addressing insomnia, work and activities, anxiety, and insight by Week 8, indicating that Escitalopram may be considered over other anti-depressants for patients with these comorbidities. Additionally, a previous randomized study reported that Escitalopram improved psychomotor functions while Amitriptyline deteriorated them[20]. Response and remission rates were also significantly better in the Escitalopram cohort.

Quality of Life is a vital outcome measure for psychiatric interventions, offering valuable insights into the burden of depressive disorders and informing intervention strategies[24]. Habits, physical changes, or medical conditions that develop during depression do not necessarily reverse when depression remits[18]. Unlike some studies suggesting no effect of second-generation antidepressants like Escitalopram and Sertraline on QoL[25], the current study demonstrated improvements in QoL with all three antidepressants by the end of the study. While Escitalopram consistently yielded better outcomes across domains, variations were noted in self-care and pain domains. Despite belonging to the same class of antidepressants, our findings underscore significant differences between Escitalopram and Sertraline in both efficacy and QoL. Suicidal ideation is more prevalent in psychiatric patients, particularly in those with depressive disorders[18,26]. Some studies have linked antidepressant use to an increase in suicidal tendency[8], especially in young individuals, potentially uncovering bipolar disorder or inducing mixed states[27]. Conversely, this study suggested a reduction in suicidal tendency among patients on antidepressants for all three cohorts. By the end of the study, no patients had suicidal ideation/behaviour in the Escitalopram cohort.

Most patients (>90% from Escitalopram and Amitriptyline cohorts; >80% from the Sertraline cohort) reported AEs.

Table 3 — *Number of patients with adverse events reported during the study in each cohort*

	Escitalopram (n=101)					Sertraline (n=87)					Amitriptyline (n=80)				
	Patients with AEs, n (%)														
	Total	G1	G2	G3	G4	Total	G1	G2	G3	G4	Total	G1	G2	G3	G4
Anxiety	13 (12.9)	2	8	3	0	17 (19.5)	0	5	12	0	1.0 (1.3)	1	0	0	0
Anorexia	23 (22.8)	14	7	1	1	26 (29.9)	4	15	7	0	5 (6.3)	2	1	2	0
Asthenia	8 (7.9)	4	3	1	0	3 (3.4)	1	2	0	0	4 (5.0)	2	1	1	0
Constipation	5 (5.0)	2	1	1	1	3 (3.4)	2	1	0	0	65 (81.3)	28	23	13	1
Decreased libido	6 (5.9)	3	2	0	1	6 (6.9)	4	1	0	0	3 (3.8)	2	0	1	0
Diarrhea	11 (10.9)	8	3	0	0	15 (17.2)	6	7	2	0	0	0	0	0	0
Dizziness	10 (9.9)	5	2	3	0	2 (2.3)	0	2	0	0	15 (18.8)	3	7	4	1
Dry mouth	12 (11.9)	6	4	1	1	8 (9.2)	2	3	3	0	49 (61.3)	22	14	13	0
Dyspepsia	19 (18.8)	7	6	3	3	21 (24.1)	3	11	7	0	6 (7.5)	3	2	1	0
Fatigue	13 (12.9)	5	5	1	2	5 (5.7)	1	4	0	0	1 (1.3)	0	1	0	0
Headache	22 (21.8)	7	6	9	0	9 (10.3)	0	6	3	0	0	0	0	0	0
Insomnia	43 (42.6)	13	17	9	4	14 (16.1)	2	4	8	0	1 (1.3)	0	1	0	0
Nausea	36 (35.6)	17	15	4	0	27 (31.0)	10	10	7	0	9 (11.3)	4	4	1	0
Somnolence	4 (4.0)	2	2	0	0	3 (3.4)	2	1	0	0	31 (38.8)	10	17	4	0
Upper abdominal pain	6 (5.9)	2	3	1	0	13 (14.9)	2	5	6	0	3 (3.8)	1	2	0	0
Vomiting	11 (10.9)	8	2	1	0	5 (5.7)	2	2	1	0	0	0	0	0	0
Giddiness	1 (1.0)	0	1	0	0	0	0	0	0	0	1 (1.3)	1	0	0	0
Irritability	1 (1.0)	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Erectile dysfunction	2 (2.0)	1	1	0	0	0	0	0	0	0	0	0	0	0	0

AE:Adverse Event, G:Grade

SSRIs commonly cause nausea and anorgasmia[18]. Previously, Escitalopram and Sertraline have induced higher AEs than other antidepressants, with Insomnia, Weight gain, and anxiety being the most common. In the current study, the most frequently reported AEs for Escitalopram were Insomnia (42.6%) and Nausea (35.6%), along with Headache, Anxiety, Fatigue and Gastrointestinal disturbances such as Anorexia, Diarrhea, Dry mouth, Vomiting and Dyspepsia (>10%). These findings align with Escitalopram's known profile, including higher incidence of headache, pruritus, memory impairment, decreased concentration, and dizziness compared to Sertraline and Fluoxetine[5], with weight gain, gastrointestinal intolerance, and sexual disturbances leading to discontinuation[28]. Although there have been case reports of akathisia[8], hyponatremia[29], mastalgia, and galactorrhea[30] induced by Escitalopram, no such cases were reported in this study. The high rate of insomnia needs to be interpreted with caution, as insomnia is also a symptom of the disease itself. Sertraline has previously demonstrated a significant reduction in appetite compared to Escitalopram[5]. Similar findings were observed in the current study with a high incidence of anorexia (>25%). Tricyclic antidepressants are associated with dry mouth and constipation[18]. As anticipated, Amitriptyline demonstrated a high incidence (>80%) of constipation and dry mouth (>60%). Most of the AEs reported during the study were Grade 1 or 2 in intensity. Unlike many studies that have reported high rates of sexual dysfunction associated with SSRIs, especially Escitalopram[28] and Sertraline[31], the rates of decreased libido were low (<10%) in the current study. Comparison of the three cohorts revealed that the rate of AEs was highest in the Amitriptyline cohort and similar between the other two.

This study had some limitations. As the discrete data for the study was collected in the real world, it was not normally distributed and did not follow normality assumptions despite being converted into logarithmic scale or percentage change. Non-parametric tests were thereby applied to the discrete data for hypothesis testing. Other limitations of the study included a small sample size and limited data on HAM-D 17 subscale scores. Additionally, the impact of confounders such as exercise or physiotherapy was not measured in the current study.

With the emergence of newer classes of antidepressants, it is necessary to continue to compare the efficacy and safety profiles of frequently prescribed drugs, especially in the real-world, which will help regulatory authorities in making sound decisions on the need for continuity or change in the treatment recommendations for depression in India.

Conclusion

Our findings indicate that all three drugs showed improvement starting at Week 2, with significant progress observed by Week 8. However, Escitalopram demonstrated higher efficacy than Sertraline and Amitriptyline, notably improving QoL and suitability for patients with anxiety and work-related disturbances. Each drug reduced suicidal tendencies with Escitalopram showing the best results. Safety profiles were consistent with known literature, with the Amitriptyline cohort reporting higher incidence of AEs.

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