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A CROSS-SECTIONAL STUDY TO EVALUATE THERAPEUTIC EFFICACY AND SAFETY PROFILE OF ESCITALOPRAM VERSUS VENLAFAXINE/DESVENLAFAXINE IN PATIENTS OF DEPRESSION IN A TERTIARY CARE HOSPITAL

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ABSTRACT: Background: Depression is a major public health disorder, with antidepressants like Selective Serotonin Reuptake Inhibitors (SSRI) and Serotonin and Norepinephrine Reuptake Inhibitors (SNRI) improving outcomes for Major Depressive Disorder (MDD) patients. However, determining which category is superior remains unclear. This study aimed to compare the efficacy and safety profile of Escitalopram (SSRI) versus Venlafaxine/Desvenlafaxine (SNRIs) in patients of depression. **Material and Methods:** An observational cross-sectional study was conducted at Outpatient Department (OPD) of Psychiatry; in 120 eligible MDD patients, already taking tablet escitalopram (10-20 mg/day) or venlafaxine (75 – 375 mg/day)/desvenlafaxine (25-100 mg/day) at least for 1 month duration. Therapeutic Efficacy was assessed by HAM-D (Hamilton rating scale for Depression) and CGI (Clinical Global Impressions) Scale. Safety profile was evaluated with the help of ASEC (Anti-Depressant Side Effect Checklist) by assessing the adverse effects experienced by patients. Independent t-test and chi square test were used to analyse quantitative and qualitative variables respectively. **Results:** Mean (±SD) scores of HAM-D and CGI scales in escitalopram group were significantly higher than venlafaxine/ desvenlafaxine group ($p<0.05$). Distribution of ASEC scores were comparable between both the studied groups. **Conclusion:** The therapeutic efficacy of venlafaxine/desvenlafaxine group was observed to be higher than that of escitalopram group. Additionally, escitalopram demonstrated a lower incidence of adverse effects in terms of safety profile. Further research is needed to validate these findings and guide revisions in current prescription practices for managing moderate to severe depression as first-line therapy.

INTRODUCTION: Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest causing social or occupational impairment [1].

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The Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) classifies the depressive disorders into five groups, namely disruptive mood dysregulation disorder, major depressive disorder (MDD), persistent depressive disorder (dysthymia), premenstrual dysphoric disorder and depressive disorder due to another medical condition [1]. World Health Organisation (WHO) has projected MDD to rank as most common cause of disease burden worldwide by 2030. DSM-5 requires presence of five of the

following symptoms, to be diagnosed with MDD, i.e., persistently low or depressed mood, decreased interest in pleasurable activities, feelings of guilt or worthlessness, lack of energy, poor concentration, appetite changes, psychomotor retardation or agitation, sleep disturbances, or suicidal thoughts [2]. About 3.8% of the population experience depression, including 5% of adults (4% among men and 6% among women), and 5.7% of adults aged above 60 years [3]. Wide range of treatment options are available for treating depression like antidepressant medications [e.g., tricyclic antidepressants (TCAs), monoamine oxidase-A inhibitors, selective serotonin reuptake inhibitors (SSRI), serotonin and norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, etc.], somatic therapies and psychotherapeutic interventions [4]. Previous studies compared SSRI to nonselective agents (primarily tricyclics), and found that SSRIs were slightly less effective than TCAs when given to inpatients but also confirmed the superior tolerability of SSRIs [5]. Thus, the introduction of SSRIs and SNRIs has undoubtedly improved outcomes in patients with MDD, but definitive evidence is still lacking on which category is superior. While comparative studies between SSRIs and SNRIs exist, direct comparisons of the two most commonly prescribed drugs in each class (Escitalopram and Venlafaxine/ desvenlafaxine) are scarce, particularly in the context of the Indian population. Therefore, a cross-sectional study was conducted to compare the efficacy and safety profiles of Escitalopram (SSRI) with Venlafaxine/ Desvenlafaxine (SNRI) antidepressants in patients with depression at a tertiary care hospital.

MATERIALS AND METHODS: An observational cross-sectional study was conducted at Outpatient Department (OPD) of Psychiatry, Rajindra Hospital, Patiala, after obtaining approval from Institute Ethics committee (approval no. BFUHS/2K21p-TH/4772). All patients diagnosed with MDD as per DSM-5 criteria, aged between 19 – 60 years (both males and females) who were already taking Tablet Escitalopram (10-20 mg/day) or Tablet Venlafaxine (75 – 375 mg/day)/ Desvenlafaxine (25-100 mg/day) at least for 1 month duration, were included in the study. Patients aged< 19 years and > 60 years, those with history of psychotic symptoms, bipolar disorder, any cardiac and hepatic diseases, comorbid chronic or terminal illnesses, known cases of pulmonary tuberculosis, HIV/AIDS, leprosy as well as pregnant and lactating mothers were excluded. After receiving written informed consent, total of 120 patients were categorized into two groups: one group of 60 patients taking Tablet Escitalopram (10-20 mg/day) & another group of 60 patients taking Tablet Venlafaxine (75 – 375 mg/day)/ Desvenlafaxine (25-100 mg/day) at least for 1 month. All the patients underwent detailed interviews and data thus collected were entered into a pretested semi-structured proforma. Therapeutic Efficacy was assessed by HAM-D (Hamilton rating scale for Depression) Scale and CGI (Clinical Global Impressions) Scale. Safety profile was evaluated by assessing the adverse effects experienced by patients with ASEC (Anti-Depressant Side Effect Checklist). The data entry was done in the Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver 21.0. Independent t-test and chi-square test were used to analyze quantitative and qualitative variables respectively. A p value of less than 0.05 was considered statistically significant.

RESULTS: In our study, distribution of age (in years) and gender was comparable between Escitalopram and Venlafaxine/Desvenlafaxine group. **Fig. 1, 2.**

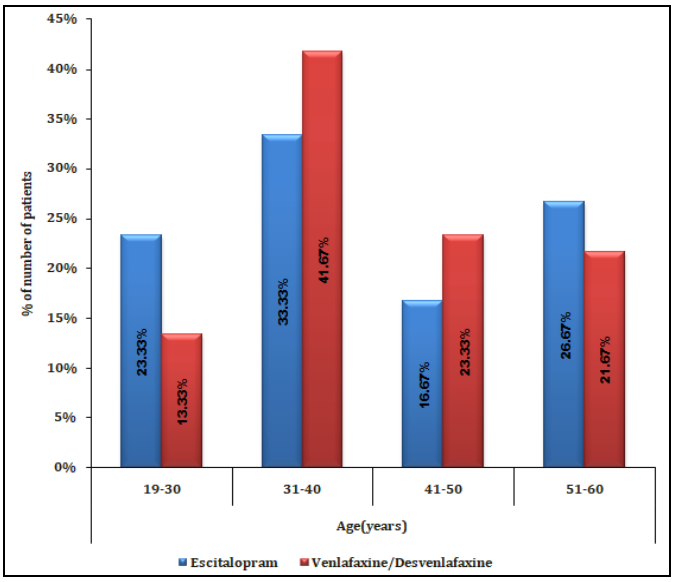

FIG. 1: COMPARISON OF AGE BETWEEN ESCITALOPRAM AND VENLAFAXINE/ DESVENLAFAXINE GROUP

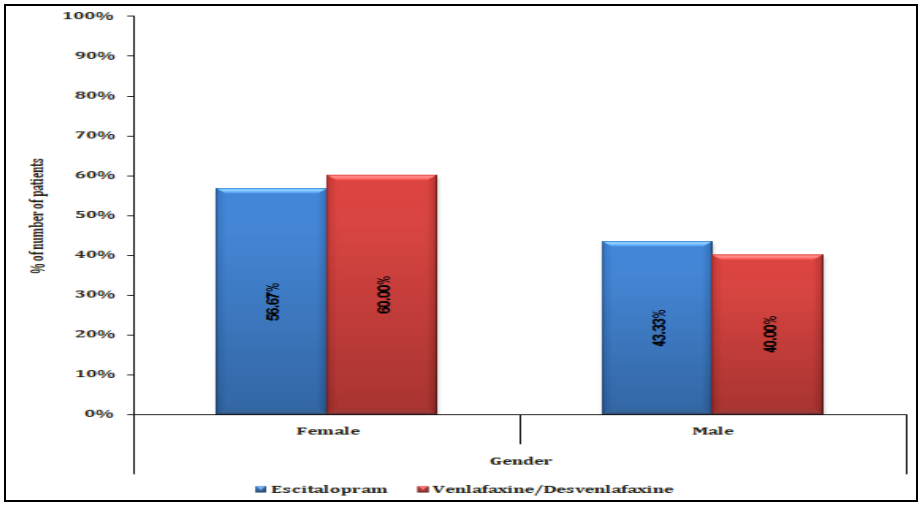

FIG. 2: COMPARISON OF GENDER BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

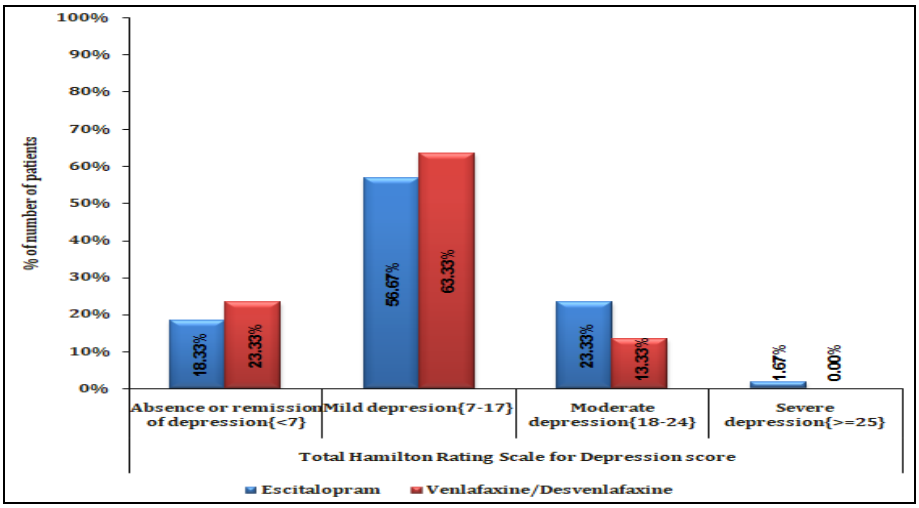

FIG. 3: COMPARISON OF TOTAL HAMILTON RATING SCALE FOR DEPRESSION (HAM-D) SCORE BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

Mean(±SD) of total Hamilton Rating Scale for Depression (HAM-D) score and of Clinical Global Impression (CGI) Scale-Severity score was significantly higher in Escitalopram group as compared to Venlafaxine/Desvenlafaxine group.(p value<0.05) **Fig. 3, 4.**

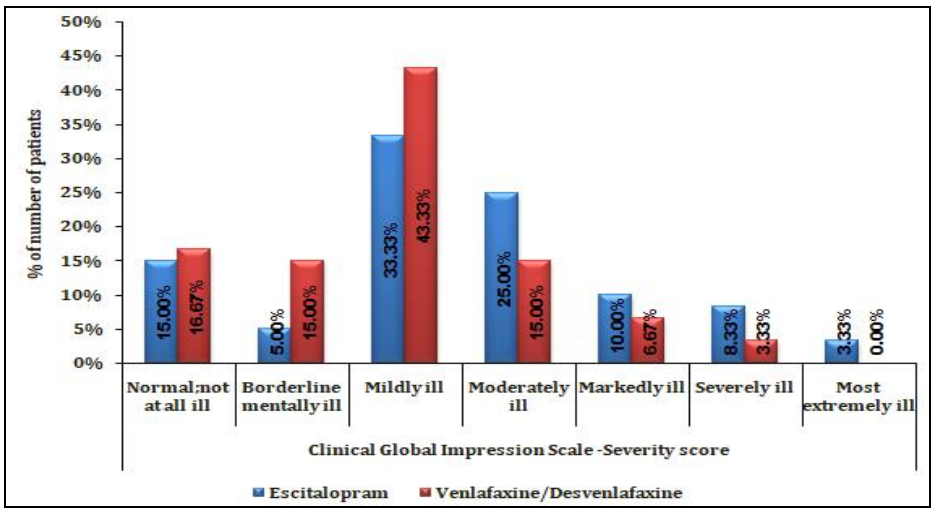

FIG. 4: COMPARISON OF CLINICAL GLOBAL IMPRESSION (CGI) SCALE- SEVERITY SCORE BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

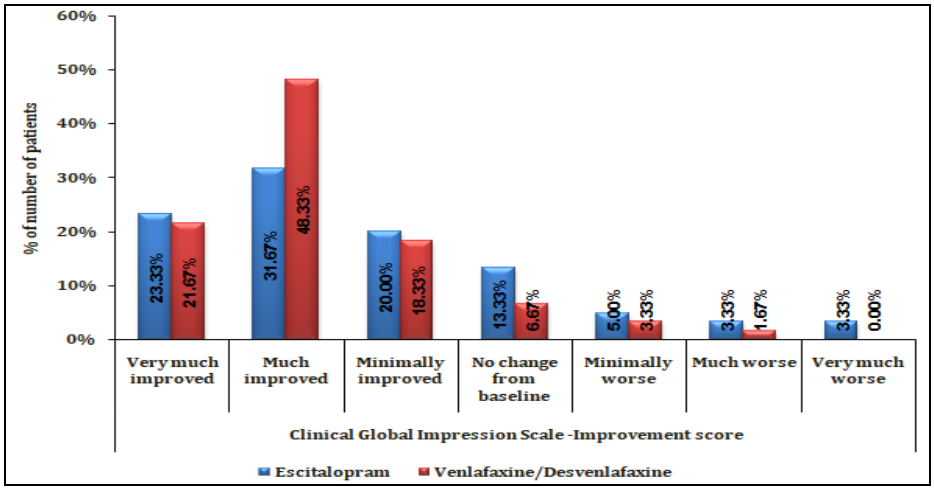

FIG. 5: COMPARISON OF CLINICAL GLOBAL IMPRESSION (CGI) SCALE-IMPROVEMENT SCORE BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

Distribution of Clinical Global Impression (CGI) Scale-Improvement score and efficacy index were comparable between both the groups with no significant difference between them. (p value>0.05) **Fig. 5, 6.**

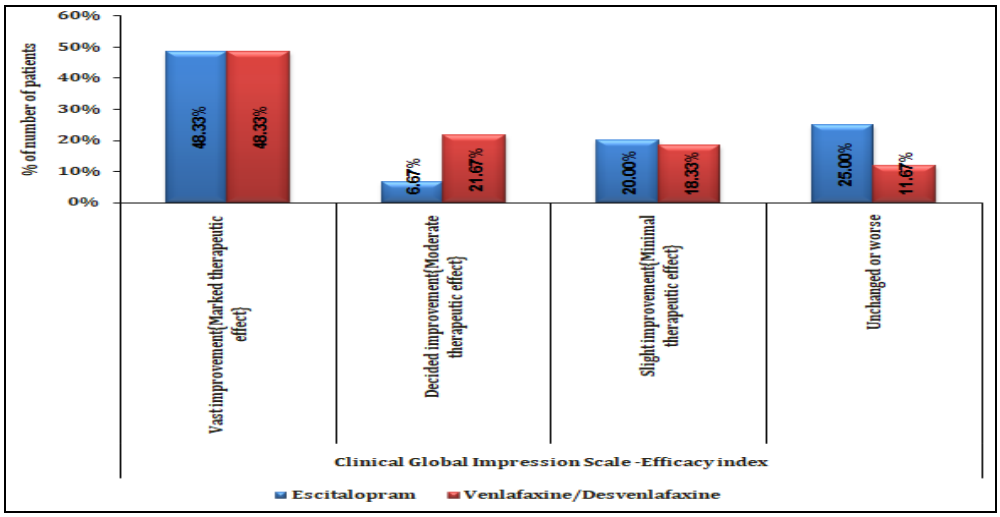

FIG. 6: COMPARISON OF CLINICAL GLOBAL IMPRESSION (CGI) SCALE-EFFICACY INDEX BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

Distribution of side-effects was comparable between both the groups. However, proportion of patients with nausea was significantly higher in Venlafaxine/desvenlafaxine group (16.67%) as compared to Escitalopram group (1.67%). (p-value <0.05) **Table 1.**

TABLE 1: COMPARISON OF SEVERITY OF ANTIDEPRESSANT SIDE-EFFECT BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

Severity of Antidepressant Side-Effect	Escitalopram (n=60)	Venlafaxine/Desvenlafaxine (n=60)	Total	P value
Headache				
Absent	55 (91.67%)	60 (100%)	115 (95.83%)	0.057†
Mild	2 (3.33%)	0 (0%)	2 (1.67%)	
Moderate	1 (1.67%)	0 (0%)	1 (0.83%)	
Severe	2 (3.33%)	0 (0%)	2 (1.67%)	
Sweating				
Absent	57 (95%)	58 (96.67%)	115 (95.83%)	1†
Moderate	1 (1.67%)	1 (1.67%)	2 (1.67%)	
Severe	2 (3.33%)	1 (1.67%)	3 (2.50%)	

Insomnia				
Absent	57 (95%)	60 (100%)	117 (97.50%)	0.244†
Moderate	2 (3.33%)	0 (0%)	2 (1.67%)	
Severe	1 (1.67%)	0 (0%)	1 (0.83%)	
Tremor				
Absent	56 (93.33%)	60 (100%)	116 (96.67%)	0.119†
Mild	1 (1.67%)	0 (0%)	1 (0.83%)	
Moderate	1 (1.67%)	0 (0%)	1 (0.83%)	
Severe	2 (3.33%)	0 (0%)	2 (1.67%)	
Drowsiness				
Absent	59 (98.33%)	56 (93.33%)	115 (95.83%)	0.428†
Moderate	0 (0%)	2 (3.33%)	2 (1.67%)	
Severe	1 (1.67%)	2 (3.33%)	3 (2.50%)	
Constipation				
Absent	59 (98.33%)	59 (98.33%)	118 (98.33%)	1†
Moderate	1 (1.67%)	1 (1.67%)	2 (1.67%)	
Diarrhoea				
Absent	59 (98.33%)	58 (96.67%)	117 (97.50%)	0.496†
Mild	1 (1.67%)	0 (0%)	1 (0.83%)	
Moderate	0 (0%)	2 (3.33%)	2 (1.67%)	
Decreased appetite				
Absent	58 (96.67%)	57 (95%)	115 (95.83%)	1†
Moderate	2 (3.33%)	2 (3.33%)	4 (3.33%)	
Severe	0 (0%)	1 (1.67%)	1 (0.83%)	
Nausea				
Absent	59 (98.33%)	50 (83.33%)	109 (90.83%)	0.021†
Mild	1 (1.67%)	5 (8.33%)	6 (5%)	
Moderate	0 (0%)	2 (3.33%)	2 (1.67%)	
Severe	0 (0%)	3 (5%)	3 (2.50%)	
Suicidal tendency				
Absent	60 (100%)	59 (98.33%)	119 (99.17%)	1†
Severe	0 (0%)	1 (1.67%)	1 (0.83%)	
Vomiting				
Absent	60 (100%)	57 (95%)	117 (97.50%)	0.244†
Moderate	0 (0%)	2 (3.33%)	2 (1.67%)	
Severe	0 (0%)	1 (1.67%)	1 (0.83%)	
Dry mouth				
Absent	55 (91.67%)	54 (90%)	109 (90.83%)	0.633†
Mild	1 (1.67%)	0 (0%)	1 (0.83%)	
Moderate	4 (6.67%)	4 (6.67%)	8 (6.67%)	
Severe	0 (0%)	2 (3.33%)	2 (1.67%)	
Disorientation				
Absent	60 (100%)	59 (98.33%)	119 (99.17%)	1†
Severe	0 (0%)	1 (1.67%)	1 (0.83%)	
Palpitations				
Absent	57 (95%)	58 (96.67%)	115 (95.83%)	1†
Mild	1 (1.67%)	0 (0%)	1 (0.83%)	
Moderate	2 (3.33%)	2 (3.33%)	4 (3.33%)	

TABLE 2: COMPARISON OF ANTIDEPRESSANT SIDE-EFFECT CHECKLIST LINKAGE BETWEEN ESCITALOPRAM AND VENLAFAXINE/DESVENLAFAXINE GROUP

Antidepressant Side-Effect Checklist linkage with Antidepressant	Escitalopram (n=18)	Venlafaxine/Desvenlafaxine (n=27)	Total	P value
No	1 (5.56%)	2 (7.41%)	3 (6.67%)	1†
Yes	17 (94.44%)	25 (92.59%)	42 (93.33%)	
Total	18 (100%)	27 (100%)	45 (100%)	

Distribution of antidepressant Side-Effect Checklist linkage with antidepressant was comparable between Escitalopram and Venlafaxine/ Desvenlafaxine group. (94.44% vs 92.59% respectively) (p value=1) **Table 2.**

DISCUSSION: Depression is a psychiatric condition that significantly impacts the socio-economic status of those affected [1]. Selecting the appropriate medication with minimal side effects and optimal efficacy is crucial. This decision is influenced by various factors including the patient's preferences, past treatment experiences, response history, and concurrent medical conditions or therapies. In our study, distribution of age (years) and gender was comparable between both the studied groups. Mean (±SD) of total HAM-D score in Escitalopram group was significantly higher as compared to Venlafaxine/Desvenlafaxine group, this finding contrasts with a study conducted by Kaur H *et al* where they reported a higher HAM-D score in the venlafaxine group (29.87 ± 10.58) as compared to the escitalopram group (21.80 ± 4.41) [7].

Mean (±SD) of CGI Scale-Improvement score was comparable between both the studied groups with no significant difference between them. However, the overall improvement observed from baseline to the end of the study was notably greater in the venlafaxine group, demonstrating an early and more substantial response. A study by Li J *et al* also observed that SNRIs were able to enhance dopamine concentrations in the medial prefrontal cortex and nucleus accumbens and induced faster antidepressant effects rather than SSRIs [8].

This could be attributed to venlafaxine's mechanism of action, which enhances both serotonin and norepinephrine levels by inhibiting their reuptake, thereby increasing their activity in the central nervous system, whereas, escitalopram primarily acts by selectively inhibiting serotonin reuptake into presynaptic nerve endings [9]. Similarly, a study by Zhou J *et al* also observed that venlafaxine produced a notably higher response rate (71%) than the SSRIs (64%) based on the CGI-Improvement score [10]. Distribution of CGI-efficacy index was comparable between both the studied groups with no significant difference between them. This was supported by the study done by Shin C *et al* which observed no significant differences in the efficacy and tolerability of escitalopram and venlafaxine or desvenlafaxine [11, 12]. However, in a study by Fagiolini *et al*, venlafaxine demonstrated superior efficacy at both primary and secondary endpoints over an 8-week period, as assessed by remission and responder rates. The enhanced efficacy of venlafaxine is attributed to its dual action compared to selective serotonin reuptake inhibitors [13]. In our study, proportion of patients with nausea was significantly lower in escitalopram group as compared to Venlafaxine/Desvenlafaxine group. This was supported by a study conducted by Kaur H *et al*, in which higher number of patients on venlafaxine reported nausea, vomiting, dry mouth, and nervousness in the first 2 weeks however these side effects were negligible after 2 weeks whereas in case of escitalopram group, patients reported greater restlessness, erectile dysfunction, and loss of libido [7].

Further, study conducted by Fagiolini *et al*, also reported higher incidences of nausea, vomiting, headache, sweating and constipation in the venlafaxine group [13]. Other previous studies also showed that use of SSRIs and SNRIs yield important side effects, such as, sexual dysfunction, bleeding, and hyponatremia, which were more prominent in antidepressants with high serotonin selectivity (SSRIs>SNRIs) [14]. In contrast, a study by Mahajan SS *et al*, observed that both escitalopram and desvenlafaxine showed comparable safety and tolerability [15].

SSRIs are generally better tolerated than other antidepressants, but common side effects may include nausea, vomiting, insomnia, drowsiness, headache, decreased sex drive, and agitation [16]. Patients with MDD are prone to amicable tolerance to escitalopram, irrespective of whether they are put on long- or short-term therapy, however, patients on venlafaxine exhibit diarrhoea and dry mouth, vertigo and constipation [17].

Available studies have shown escitalopram as an effective first-line treatment option for patients experiencing episodes of depression based on its affordability [18]. However, venlafaxine, an SNRI with dual action involving serotonergic and noradrenergic mechanisms may also offer potential

advantages in terms of efficacy and tolerability, making it a compelling candidate for consideration as a first-line antidepressant in routine clinical practice. Moreover, the marginal difference in efficacy observed between the two groups in our study did not allow for a clear determination of its clinical relevance. Therefore, further studies are needed to rigorously assess whether differences in efficacy between these treatments are more pronounced across diverse study populations. The study generates data regarding the use of escitalopram and venlafaxine/desvenlafaxine in north Indian population, with the help of three validated scales, which adds to the strength of our study.However, restricted study population and study setting, deprivation of placebo group, not including other drugs from SSRI and SNRI group, pose limitations to our study which could be overcome by conducting further studies in this regard.

CONCLUSION: Our study concludes that Venlafaxine/Desvenlafaxine exhibits higher therapeutic efficacy compared to Escitalopram, although Escitalopram demonstrates a lower incidence of adverse effects in terms of safety profile. There is a pressing need for further research in this area which could potentially revise current prescription practices for first-line management of moderate to severe depression using antidepressants.

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CONFLICT OF INTEREST: The authors have no conflict of interest to disclose.

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