

ORIGINAL RESEARCH

A Study to evaluate effect of Escitalopram on High Sensitivity C-Reactive Protein (hs-CRP) levels in Patients of depression with suicidal behaviour

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ABSTRACT

Background: Depression is a prevalent mood disorder characterized by persistent sadness and a lack of interest in activities, significantly impacting daily life. It is often accompanied by suicidal behavior, and inflammation markers like high-sensitivity C-reactive protein (hs-CRP) have been linked to its severity. Escitalopram, a selective serotonin reuptake inhibitor (SSRI), is commonly used in treating major depressive disorder (MDD). **Method:** This prospective interventional study was conducted at Mahatma Gandhi Memorial Medical College and MY Hospital, Indore, over 18 months. It involved 60 adult patients diagnosed with depression and suicidal behavior, as per ICD-10 criteria. Participants were drug-naïve or drug-free for three months prior to the study. The study assessed changes in hs-CRP levels and depression severity using the Hamilton Depression Rating Scale (HAM-D) before and after four weeks of escitalopram treatment. **Results:** The study found a significant reduction in hs-CRP levels from baseline (1.10 ± 0.97 mg/L) to the fourth week (0.91 ± 0.038 mg/L) post-treatment ($p < 0.001$). Depression severity also decreased significantly, as indicated by HAM-D scores dropping from 25.26 ± 5.937 at baseline to 14.78 ± 4.720 at the fourth week ($p < 0.001$). These reductions were consistent across various demographic groups, including age, gender, marital status, and education level. **Conclusion:** Escitalopram effectively reduces hs-CRP levels and alleviates depressive symptoms in patients with suicidal behavior. The reduction in hs-CRP levels is independent of its antidepressant effects, suggesting potential anti-inflammatory benefits of escitalopram in treating depression.

Keywords: Depression, Suicidal Behavior, Escitalopram, High-sensitivity C-reactive protein (hs-CRP), Inflammation, Hamilton Depression Rating Scale (HAM-D).

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INTRODUCTION

Depressive disorder, or depression, is a mood disorder that causes persistent sadness and decreased activity. It harms all aspects of life. [1] Depression is the fourth leading cause of disability worldwide, according to WHO. Depression affects 3.8% of the population, or 10% of adults (4% men and 6% women). Nearly 280 million people worldwide suffer from depression. [2] Depression has a lifetime prevalence of 20%–25% in women and 7%–12% in men. [3] Depression symptoms include a depressed mood, sleep changes, anhedonia, psychomotor retardation, decreased appetite, libido, weight loss, feelings of worthlessness, suicidal ideation, and suicide attempts, but not all are necessary for diagnosis. If symptoms last at least two

weeks and dominate the day, ICD-10 and DSM V diagnose a depressive episode. Anxiety and psychotic symptoms like delusions and hallucinations may accompany these symptoms. The American Psychiatric Association sorts depression into these categories: Disruptive Mood Dysregulation Disorder, Dysthymia, Major Depression, Premenstrual Dysphoric Disorder, and Medically caused Depression. [5] Major Depressive Disorder (MDD) patients often consider suicide. Depressive episodes are associated with 15% suicide risk and suicidal ideation and behaviour. 29% and 69% of MDD patients were suicidal. [7] Research shows that inflammation is a major factor in psychiatric disorders, suggesting that dysfunctional immunological and inflammatory systems may cause

them. Mood disorders, schizophrenia, anxiety, and post-traumatic stress disorder raise CRP. CRP levels above 3 mg/L are associated with worsening psychopathological symptoms, mental illness progression, and treatment resistance.[6] CRP levels above 3 mg/L may cause cerebral inflammation by decreasing neurotrophic support, increasing glutamatergic excitotoxicity, oxidative stress, and neuronal serotonin transporter activity, resulting in microstructural disintegration primarily in frontal pathways and executive function. Also, it may affect dopaminergic neurones involved in psychomotor speed, memory, and executive cognitive abilities. Thus, anti-inflammatory treatments may improve depression-related cognition. Research has found elevated CRP and pro-inflammatory cytokines in suicide attempters.[8] The lower detection threshold of high-sensitivity CRP (hs-CRP) makes it a potential marker for subclinical low-level inflammation.[9] Low-concentration detection and a brief half-life make high-sensitivity CRP (hs-CRP) a good research alternative. Depression management may involve psychotherapy, pharmacotherapy, or a combination of both [10]. [11] Doctors often prescribe escitalopram for Major Depressive Disorder. [12] Escitalopram, an FDA-approved medication, treats major depressive disorder (unipolar), obsessive-compulsive disorder, generalised anxiety disorder, social anxiety disorder, panic disorder, and premenstrual dysphoric disorder worldwide. [13] It is the active S-enantiomer of SSRI. It binds to two sites on the sodium-dependent serotonin transporter protein (SERTs): the primary site, which regulates nerve ending serotonin reuptake, and the allosteric site, which induces SERT conformational changes. [14, 15, 16] SSRIs may reduce depression symptoms, but they may also increase suicide attempts and deaths, especially in younger people. [17, 18] SSRI treatment may reduce the risk of suicidal behaviour in youth and adults, according to some studies. [19] In SSRI-treated patients, monitoring CRP levels may help assess suicidal behaviour. Pre-treatment CRP levels affect treatment response, according to limited research. [20] Therefore, CRP levels can indicate treatment efficacy and help predict outcomes. Thus, this study compares HsCRP levels before and after Escitalopram.

MATERIAL & METHODS

The present study was conducted to evaluate the effect of Escitalopram on hs-CRP Levels in patients of Depression with suicidal behaviour.

Study site- Department of Psychiatry, Mahatma Gandhi Memorial Medical College and MY Hospital, Indore (Madhya Pradesh).

Study design- Prospective, Interventional study.

Study duration- 18 months (from August 2022 to December 2023).

Study population- patients with the diagnosis of Depression (F32 Depressive Episode or F33

Recurrent Depressive Episode, except depression with psychotic symptoms) according to ICD-10-Diagnostic Criteria for Research (DCR) with suicidal behavior.

Selection criteria

Inclusion criteria

1. Adults aged 18-60 years.
2. Patients who were drug naïve or drug-free for 3 months.
3. Willing to participate in the study.

Exclusion criteria

- Patients of Depression with Psychotic symptoms, or any other psychiatric comorbidity (schizoaffective bipolar affective disorder).
- Patients with medical inflammatory and neurological comorbidities (rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease).
- Patients with HIV infection, neurodegenerative disorders, Alzheimer's disease, Huntington's disease, Parkinson's disease, and multiple sclerosis).
- Patients currently using interferon—based immunotherapy, anti-psychotics, anti-depressant, mood stabilizers, or drug-free < 3 months.
- Patients treated with non-steroidal anti-inflammatory drugs, statins, steroids, and antibiotics, anti-hypertensive drugs, growth hormones, retinoids, immunomodulators due to their modifying effects on CRP levels.
- Patients with a history of suicidal attempts or non-suicidal self-harm behavior in the last year.
- Patients with medical co-morbidity (s) including Hypertension, or any endocrinological disorder (hypothyroidism, hyperthyroidism, Cushing syndrome, diabetes mellitus), neoplasm, or any chronic inflammatory disorder.
- Pregnant or lactating females.
- Patients undergoing hemodialysis.

Sample size- Sample size was estimated using G*Power software version 3.1.9.6.

The input parameters:

Effect size- 0.5 (Medium, according to Cohen)

α probability error- 0.05

Power (1- β error probability)- 95%

Number of groups- 1 (before and after comparison)

Output parameters:

Critical t- 2.005

Sample size- 54

Adjusting the sample size for drop-out (10%),

Sample size= $54/(1-0.1) = 60$.

Thus, 60 subjects were included in the study.

Sampling technique- Convenience sampling technique.

Methodology- The study was initiated after approval from the institutional ethics committee. Depression patients with suicidal behavior visiting the OPD/IPD

of the department and meeting the inclusion criteria were included in the study.

A detailed physical examination was done to rule out any medical or neurological abnormality.

Data collection

The demographic details of the patients including age, gender, marital status, socioeconomic status, and locality were recorded. A history of the age of onset of illness, duration of illness, and number of episodes of MDD was recorded.

The diagnosis of depression was made using the International Classification of Diseases (ICD-10) and Hamilton Depression Rating Scale (HAM-D)[25]. The suicidal behavior was assessed using The Suicide Behaviours Questionnaire-Revised (SBQ-R).[56] 45 | Page

For the estimation of hs-CRP, a 5ml blood sample was collected in a clot activator (red top) tube. The serum was processed from the sample via a centrifuge machine and the serum was analyzed with an Automated analyzer using the Immunoturbidimetry method. hs-CRP levels were assessed at baseline (before administration of the drug) and 4 weeks after the administration of escitalopram 10 mg. HAM-D was also evaluated at baseline, 2-week, and 4-week

follow-up. Those having active suicidal behavior were dropped out of the study.

The data was collected in a predesigned proforma.

Statistical analysis plan- Data was analyzed using SPSS (Statistical Package for Social Sciences) 25.0 version, IBM, Chicago. Data were analyzed for probability distribution using the Kolmogorov-Smirnov test. Descriptive statistics were performed. Intra-group comparison of continuous variables was done using paired t-test and Repeated measures ANOVA, followed by post hoc analysis, if needed. Inter-group comparison of continuous variables was done using an Independent t-test and/or One-way ANOVA. Inter-group comparison of categorical variables was done using the Chi-square test. P-value <.05 was considered statistically significant.

Ethical considerations- The study was initiated after approval from the institutional ethics committee of Mahatma Gandhi Memorial Medical College, Indore. The participants of the study were informed about the purpose of the study and the procedures involved in it. The participants were informed that their participation was voluntary and they had the right to quit at any point in time. Written informed consent was obtained from the subjects willing to participate in the study. Confidentiality of the information was maintained.

RESULT

Table -1 Sociodemographic Profile of Study Participants

Characteristic	Category	Number of Subjects	Percentage (%)
Age Group	18-30 years	27	45.0
	31-40 years	14	23.3
	41-50 years	12	20.0
	51-60 years	7	11.7
Gender	Male	31	51.7
	Female	29	48.3
Marital Status	Married	31	51.7
	Remarried	1	1.7
	Widowed	8	13.3
	Divorced	3	5.0
	Unmarried	17	28.3
Education	Illiterate	2	3.3
	Primary school	6	10.0
	Middle school	10	16.7
	Higher school	10	16.7
	Intermediate school/Diploma	10	16.7
	Graduate	18	30.0
Occupation	Professional degree	4	6.7
	Unemployed	25	41.7
	Elementary occupation	5	8.3
	Plant & machine operator & assembly	1	1.7
	Craft & related	7	11.7
	Skilled agriculture and fishery	5	8.3
	Skilled worker, shop and market	3	5.0
	Clerk	2	3.3
	Technician/Associate professional	6	10.0
	Professional	6	10.0
Socioeconomic Status	Legislators/Senior officials/Managers	0	0.0
	Upper	2	3.3

	Upper middle	25	41.7
	Lower middle	15	25.0
	Upper lower	18	30.0
	Lower	0	0.0
Family Type	Nuclear	37	61.7
	Joint	23	38.3
Locality	Urban	39	65.0
	Rural	21	35.0

This table presents a demographic details of subjects across various characteristics, including age, gender, marital status, education, occupation, socioeconomic status, family type, and locality. The majority of participants (45.0%) are aged 18-30 years, with males representing 51.7% and females 48.3% of the group. Most are married (51.7%), and the predominant

educational level is graduate (30.0%). The largest occupational group is unemployed (41.7%), while most subjects belong to the "upper middle" socioeconomic status (41.7%). Nuclear families are more common (61.7%), and a higher proportion of subjects live in urban areas (65.0%) compared to rural ones.

Table-2 Pre & Post treatment Comparison of symptoms at 2 week and 4 week

Characteristic	Category	Mean \pm Standard Deviation	Number of Subjects	Percentage (%)	t/F Value	P Value
Hamilton Depression Rating Scale	At baseline	25.26 \pm 5.937			211.776	<.001*
	At 2nd week	18.7 \pm 5.270				
	At 4th week	14.78 \pm 4.720				
Suicide Behaviour Questionnaire (SBQ) Score	<7		7	11.7		
	\geq7		53	88.3		
	Total		60	100.0		
Total Duration of Illness	<12 weeks		19	31.7		
	12-24 weeks		29	48.3		
	>24 weeks		12	20.0		
	Total		60	100.0		
hs-CRP Levels	At baseline	1.10 \pm 0.97			40.682	<.001*
	At 4th week	0.91 \pm 0.038				

Note:

- A repeated measure ANOVA was used for the Hamilton Depression Rating Scale, and a paired t-test was used for hs-CRP levels.
- *P-value < .05 was considered statistically significant.

This table summarizes various clinical measures and their statistical significance in the study. The Hamilton Depression Rating Scale (HDRS) shows a decrease in mean scores from baseline (25.26 \pm 5.937) to the 2nd week (18.7 \pm 5.270) and the 4th week

(14.78 \pm 4.720), with a significant change (t/F value: 211.776, *P* < 0.001). Suicide Behavior Questionnaire (SBQ) scores indicate that 88.3% of subjects score \geq 7, suggesting a high risk group. Duration of illness spans <12 weeks (31.7%), 12-24 weeks (48.3%), and >24 weeks (20.0%). High-sensitivity C-reactive protein (hs-CRP) levels reduce from baseline (1.10 \pm 0.97) to the 4th week (0.91 \pm 0.038), also showing significant change (*P* < 0.001).

Table- 3 Correlation and Comparison of hs-CRP Levels

Characteristic	Category	hs-CRP Levels (Mean \pm SD)	t/F-Value	p-Value
Correlation	Age & hs-CRP	r = 0.609		<0.001*
	Age & Change in hs-CRP	r = 0.299		0.020

Gender	Male (Baseline/4th Week/Change)	1.24 ± 1.098 / 1.06 ± 1.003 / 0.17 ± 0.081	5.392	<0.001*
	Female (Baseline/4th Week/Change)	0.95 ± 0.007 / 0.74 ± 0.066 / 0.21 ± 0.011	4.029	<0.001*
	Inter-group comparison	t = 0.977 / 1.196 / -0.580	0.333/0.237/0.564	
Marital Status	Married	1.16 ± 0.262 / 0.98 ± 0.164 / 0.18 ± 0.038	4.305	<0.001*
	Widowed	1.72 ± 1.022 / 1.41 ± 1.087 / 0.31 ± 0.185	3.101	0.017*
	Divorced	0.31 ± 0.075 / 0.23 ± 0.037 / 0.07 ± 0.002	1.429	0.289
	Unmarried	0.83 ± 0.105 / 0.66 ± 0.065 / 0.17 ± 0.010	3.465	0.003*
	Inter-group comparison	F = 1.709 / 1.456 / 0.996	0.176/0.236/0.401	
Family Type	Nuclear	1.15 ± 1.023 / 0.96 ± 0.074 / 0.18 ± 0.033	4.885	<0.001*
	Joint	1.01 ± 0.294 / 0.81 ± 0.149 / 0.20 ± 0.038	4.019	0.001*
	Inter-group comparison	t = 0.469 / 0.554 / -0.194	0.640/0.582/0.847	
Locality	Urban	1.13 ± 1.025 / 0.97 ± 0.199 / 0.15 ± 0.102	5.45	<0.001*
	Rural	1.04 ± 0.320 / 0.79 ± 0.122 / 0.25 ± 0.002	3.833	0.001*
	Inter-group comparison	t = 0.267 / 0.622 / -1.494	0.791/0.537/0.140	
Education	Illiterate	2.08 ± 1.583 / 1.59 ± 0.947 / 0.49 ± 0.036	1.089	0.473
	Primary school	1.03 ± 0.944 / 0.85 ± 0.247 / 0.18 ± 0.098	2.245	0.075
	Middle school	1.66 ± 0.721 / 1.32 ± 0.539 / 0.34 ± 0.138	3.226	0.010*
	Higher school	0.73 ± 0.267 / 0.56 ± 0.183 / 0.17 ± 0.086	2.965	0.016*
	Intermediate/diploma	1.03 ± 0.145 / 0.90 ± 0.202 / 0.12 ± 0.067	2.433	0.038*
	Graduate	0.95 ± 0.060 / 0.82 ± 0.077 / 0.13 ± 0.071	3.258	0.005*
	Professional degree	1.07 ± 0.703 / 0.91 ± 0.194 / 0.15 ± 0.005	12.318	0.001*
Inter-group comparison	F = 0.903 / 0.595 / 1.721	0.500/0.733/0.134		
Employment Status	Unemployed	0.70 ± 0.271 / 0.52 ± 0.031 / 0.17 ± 0.027	3.811	0.001*
	Employed	1.39 ± 1.195 / 1.18 ± 1.011 / 0.20 ± 0.040	5.070	<0.001*
	Inter-group comparison	t = -2.437 / -2.529 / -0.526	0.018*/0.014*/0.601	

The correlation and comparison of high-sensitivity C-reactive protein (hs-CRP) levels were analyzed across different variables, revealing significant findings. Age positively correlated with both hs-CRP levels and its change over time. Gender, marital status, family type, locality, education, employment status, and duration of illness significantly influenced hs-CRP levels. Higher levels were observed in males, employed

individuals, widowed patients, and those with longer durations of illness. Urban residents and those with higher educational levels showed significant intra-group reductions in hs-CRP. Statistical significance was determined using Pearson's correlation, paired t-tests, independent t-tests, and one-way ANOVA (p-value < 0.05).

Table- 4 hs-CRP Levels and Duration of Illness with Post Hoc Analysis and Correlation

Analysis	Category/Comparison	hs-CRP Levels (Mean \pm SD)	t/F-Value	p-Value
Duration of Illness	<12 weeks	0.56 \pm 0.118 / 0.41 \pm 0.164 / 0.15 \pm 0.079	3.729	<0.001*
	12-24 weeks	1.16 \pm 1.041 / 0.92 \pm 0.087 / 0.23 \pm 0.074	4.638	<0.001*
	>24 weeks	1.80 \pm 1.046 / 1.65 \pm 1.172 / 0.14 \pm 0.097	2.598	0.025*
	Inter-group comparison	F = 5.193 / 6.250 / 0.982	0.008* / 0.004* / 0.381	
Post Hoc Analysis	<12 weeks vs. 12-24 weeks	0.219 / 0.261		
	<12 weeks vs. >24 weeks	0.001* / <0.001*		
	12-24 weeks vs. >24 weeks	0.041* / 0.011*		
Correlation (hs-CRP & HAMD)	Percentage change in hs-CRP & HAMD	r = 0.128		0.330

The analysis of hs-CRP levels based on the duration of illness shows significant intra-group reductions across all categories. Baseline levels of hs-CRP were highest in subjects with >24 weeks of illness, while the greatest reduction in hs-CRP occurred in the 12-24 weeks group. Post hoc comparisons reveal statistically significant differences between <12 weeks vs. >24 weeks and 12-24 weeks vs. >24 weeks. A weak and non-significant correlation ($r = 0.128$, $p = 0.330$) was observed between the percentage change in hs-CRP and HAMD scores. Statistical significance was determined using t-tests, ANOVA, and post hoc analysis (p -value < 0.05).

DISCUSSION

Depression is a widespread mental ailment that affects all aspects of life.[2] Major depressive disorder patients had 29%–69% suicidal feelings across cohorts.[7] Immune-inflammatory pathways may play a major role in SB development.[8] Neuropsychiatric diseases are associated with chronic central and peripheral inflammation.[21] In suicidal patients, blood and cerebrospinal fluid include higher levels of inflammatory cytokines such IL-1 beta and IL-6. Suicidal people have lower plasma and cerebral fluid IL-8 levels. Suicidal intent is linked to plasma CRP.[22] Previous study on CRP levels in suicidal people has found contradictory results. Some research found no correlation between CRP and suicidal behavior, whereas others found strong associations in mental conditions. This study evaluates how Escitalopram, the preferred MDD treatment, affects hs-CRP levels in depressed and suicidal patients.

This study included 60 depressed people. The average age of the subjects was 34.6 ± 12.334 years, with 45.0% in the 18-30 age range. This study confirmed a thorough nationwide survey of Indian individuals that found the highest number of adults with depressive disorders were aged 18–29.[23] Suicidal people showed a similar pattern. Young people aged 18–30 committed 34.5% of suicides.[24] Males outnumbered girls 51.7% to 48.3% in this study. This illustrates

India's depression and suicide tendency. In Singh OP et al. (2022), male suicide rates were higher than female. The economic slump has hit men hardest, as they are the family's main financial providers. They have suffered salary cuts, payment interruptions, and even unemployment.[24] Mudgal V et al. (2020) found that men are more suicidal than women.[25] The majority of research participants (51.7%) were married. Rane A. et al. (2014) found similar results.[26] In India, women can marry at 18 and males at 21, with 18 to 30 being the most popular.[27] The majority of research participants (41.7%) were unemployed. Major clinical depression is more likely in unemployed individuals.[28] Many participants (41.7%) were upper middle class. Most subjects (61.7%) were nuclear families. Urban residents comprised 65.0% of participants. Rane A et al. (2014) found that urbanites are most suicidal. [26] The Hamilton Depression Rating Scale, a long-standing and frequently used tool for assessing depression severity in research and clinical settings, has strong inter-rater reliability with ICCs of 0.923 to 0.967.[29] Thus, the Hamilton Depression Rating Scale assessed research participants' depression. This study used the SBQ-R to assess suicidal behavior. Previous study has shown that the SBQ-R can identify suicide risk.[30]

Escitalopram, an FDA-approved medicine, treats major depressive disorder (unipolar), obsessive-compulsive disorder, generalized anxiety disorder, social anxiety disorder, panic disorder, and premenstrual dysphoric disorder worldwide.[13] SSRIs may reduce depressive symptoms, but they may also increase suicide attempts and deaths, especially in younger people.[17, 18] SSRI medication may reduce the risk of suicide behavior in kids and adults, according to various studies.[19] In SSRI-treated patients, monitoring CRP levels may help determine suicidal behavior. Thus, this study evaluates Escitalopram's impacts.

The study found that Escitalopram medication significantly reduced the baseline Hamilton

Depression Rating Scale score from 25.2 ± 5.937 to 18.7 ± 5.270 by the second week and 14.78 ± 4.720 by the fourth week. Escitalopram reduced HAM-D score, proving its depression treatment efficiency. Kirino et al. (2012) found that escitalopram prevented major depressive disorder relapse better than placebo.[31] Jiang K et al. (2017) conducted a 24-week, open-label, prospective, single-arm study. The HAM-A scale assessed depression. The baseline HAM-A score was $27.6 (\pm 7.26)$, but considerably dropped to $6.0 (\pm 8.39)$ at 24 weeks.[32] In a multicenter, randomized, double-blind, placebo-controlled experiment, Wang X et al. (2021) found that escitalopram significantly reduced HAM-D17 ratings over 8 weeks, while the placebo group showed only a minor reduction. The hs-CRP level was 1.10 ± 0.97 at baseline and 0.91 ± 0.038 in the fourth week in the current study [3]. There was a significant drop in hs-CRP levels after four weeks of treatment with escitalopram (p -value < 0.05). Even without improving depression symptoms, escitalopram decreased CRP levels in MDD patients, according to O'Brien et al. (2006).[33] Chavda N et al. (2010) found that newly diagnosed depression patients had higher CRP, ESR, and WBC counts. SSRIs like fluoxetine and escitalopram also reduced these indicators without reducing depression.[34] The 51-60 year age group had the highest baseline hs-CRP levels, followed by the 41-50 year group, the 31-40 year group, and the 18-30 year group. Pearson's correlation coefficient showed a considerable positive association between age and hs-CRP levels. This observation is based on chronic inflammation and aging. Chronic inflammation causes many age-related disorders, including arthritis and type 2 diabetes.[35,36] Age did not affect hs-CRP levels in this study ($p > 0.05$). Escitalopram worked regardless of age.

Males had greater hs-CRP levels than females, although the difference was not statistically significant (p -values $> .05$). Males' higher baseline hs-CRP levels are due to their higher prevalence of chronic inflammatory illnesses like periodontitis and harmful habits like tobacco and alcohol usage.[37,38] Results showed a substantial decrease in hs-CRP levels in both males and females after therapy (p -value < 0.05). This showed that Escitalopram works for men and women. At baseline and the fourth week post-treatment, widowed individuals had the highest hs-CRP levels, followed by married individuals, unmarried individuals, and divorced individuals, but the differences were statistically non-significant (p -value $> .05$). After therapy, hs-CRP levels significantly decreased in married, divorced, and unmarried individuals (p -value $< .05$). However, widowed people showed no significant change ($p > 0.05$). Widows' high hs-CRP levels indicate that marriage breakdown harms mental health. Marital disturbance in midlife or later can harm health, especially psychological well-being, in the near run,

according to Ding D et al. (2021).[39]Srivastava S et al. (2021) found that bereaved elderly individuals living alone were 56% more likely to be depressed.[40]Marriage may protect against suicide by increasing social and interpersonal support, according to Mudgal V et al. (2020).[25] The current study found a substantial reduction in hs-CRP levels in all categories except the divorced group, which had a smaller sample size. Escitalopram worked for all subjects, regardless of marital status, by lowering hs-CRP.

At baseline and four weeks post-treatment, nuclear and combined family members had similar hs-CRP levels (p -values > 0.05). The groups also had similar hs-CRP changes ($p > 0.05$). Post-treatment, hs-CRP levels significantly decreased in both family types (p -value $< .05$). This suggested family type did not affect hs-CRP levels. Escitalopram reduced hs-CRP in both groups, proving its efficacy regardless of family type. Locality did not substantially affect baseline and four-week post-treatment hs-CRP levels in urban and rural subjects (p -values $> .05$). Escitalopram was effective across all participants, regardless of locality, since both groups showed a substantial drop in hs-CRP levels (p -value > 0.05).

The study found no significant differences in baseline, fourth-week post-treatment, or decrease in hs-CRP levels across educational categories. Escitalopram reduced hs-CRP levels significantly in other categories but not in illiterates and primary school students. Poor treatment protocol adherence may explain it. Studies show that illiteracy reduces drug adherence.[41]

Compared to unemployed individuals, employed individuals had significantly higher hs-CRP levels at baseline and four weeks post-treatment (p -value $< .05$). The difference in hs-CRP levels between groups was not significant ($p > 0.05$). After therapy, both groups showed a substantial decrease in hs-CRP levels compared to baseline (p -value $< .05$). The current investigation indicated that employed subjects had higher hs-CRP levels than jobless subjects, even though unemployed people have higher depression rates [28]. This gap may be due to higher anxiety, depression, and work-related pressures in employed people.[42] Escitalopram reduced hs-CRP in all subjects, independent of job status.

In this study, HAM-D and HsCRP levels did not correlate. Escitalopram may affect depression and inflammation incompatibly. Escitalopram fights depression via binding to the sodium-dependent serotonin transporter protein (SERT) in the presynaptic neurone, not by reducing inflammation.[13] SSRI medication significantly reduced CRP levels in MDD patients (p -value $< .0001$), regardless of depression relief.[33] Chavda N et al. found that newly diagnosed depression patients had higher CRP, ESR, and WBC counts. SSRIs like fluoxetine and escitalopram lowered these indicators without antidepressant effects.[34]

Independent of their antidepressant characteristics, antidepressants reduce inflammation, according to Rothermundt M et al. (2001)[43], Kenis G et al. (2002)[44], and Sinead M et al. (2006)[45].

CONCLUSION

Current study shows Escitalopram dramatically lowers hs-CRP in depressed suicidal patients. Escitalopram affects hs-CRP regardless of its antidepressant qualities. Escitalopram works in all age, gender, marital status, geographical, and educational groups. Escitalopram dramatically lowers hsCRP and HAMD, although this is mutually exclusive.

REFERENCES

- Kessler RC, Bromet EJ. The epidemiology of depression across cultures. *Annual review of public health*. 2013 Mar 18;34(1):119-38.
- WHO. Depressive disorder (depression) (who.int)
- Wang X, Fan Y, Li G, Li H. The efficacy of escitalopram in major depressive disorder: a multicenter randomized, placebo-controlled double-blind study. *Int Clin Psychopharmacol*. 2021;36(3):133-139.
- Szałach ŁP, Lisowska KA, Cudała WJ. The Influence of Antidepressants on the Immune System. *Arch Immunol Ther Exp (Warsz)*. 2019;67(3):143-151.
- Chand SP, Arif H. Depression. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; July 17, 2023.
- Orsolini L, Latini R, Pompili M, et al. Understanding the Complex of Suicide in Depression: from Research to Clinics. *Psychiatry Investig*. 2020;17(3):207-221.
- Rentería, M., Schmaal, L., Hibar, D. et al. Subcortical brain structure and suicidal behaviour in major depressive disorder: a meta-analysis from the ENIGMA-MDD working group. *Transl Psychiatry* 2017;7:e1116.
- Miola A, Dal Porto V, Tadmor T, et al. Increased C-reactive protein concentration and suicidal behavior in people with psychiatric disorders: A systematic review and meta-analysis. *Acta Psychiatr Scand*. 2021;144(6):537-552.
- Han E, Fritzer-Szekeres M, Szekeres T, Gehrig T, Gyöngyösi M, Bergler-Klein J. Comparison of High-Sensitivity C-Reactive Protein vs C-reactive Protein for Cardiovascular Risk Prediction in Chronic Cardiac Disease. *J Appl Lab Med*. 2022;7(6):1259-1271.
- Toffol E, Miola A, Magnolfi G, Trevisan G, Scocco P. High hs-CRP levels after an attempted suicide: A matched case-control study. *Journal of Affective Disorders reports*. 2022;10:100381.
- Zimmerman M, Sheeran T, Young D. The Diagnostic Inventory for Depression: a self-report scale to diagnose DSM-IV major depressive disorder. *Journal of clinical psychology*. 2004;60(1):87-110.
- Masilamani S, Ruppelt SC. Escitalopram (Lexapro) for depression. *Am Fam Physician*. 2003;68(11):2235-2236.
- Landy K, Rosani A, Estevez R. Escitalopram. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; November 10, 2023.
- Chen F, Larsen MB, Neubauer HA, Sanchez C, Plenge P, Wiborg O. Characterization of an allosteric citalopram-binding site at the serotonin transporter. *J Neurochem*. 2005;92(1):21-28.
- Neubauer HA, Hansen CG, Wiborg O. Dissection of an allosteric mechanism on the serotonin transporter: a cross-species study. *Mol Pharmacol*. 2006;69(4):1242-1250.
- Sanchez C, Bogeso KP, Ebert B, Reines EH, Braestrup C. Escitalopram versus citalopram: the surprising role of the R-enantiomer. *Psychopharmacology (Berl)*. 2004;174(2):163-176.
- Hetrick SE, McKenzie JE, Cox GR, Simmons MB, Merry SN. Newer generation antidepressants for depressive disorders in children and adolescents. *BJPsych Advances*. 2012;11(11):CD004851.
- Stone M, Laughren T, Jones ML, Levenson M, Holland PC, Hughes A, et al. Risk of suicidality in clinical trials of antidepressants in adults: analysis of proprietary data submitted to US Food and Drug Administration. *Bmj*. 2009;339:b2880.
- Lagerberg T, Fazel S, Sjölander A, Hellner C, Lichtenstein P, Chang Z. Selective serotonin reuptake inhibitors and suicidal behaviour: a population-based cohort study. *Neuropsychopharmacology*. 2022;47(4):817-823.
- Uher R, Tansey KE, Dew T, Maier W, Mors O, Hauser J, Dernovsek MZ, Henigsberg N, Souery D, Farmer A, McGuffin P. An inflammatory biomarker as a differential predictor of outcome of depression treatment with escitalopram and nortriptyline. *American Journal of Psychiatry*. 2014 Dec 1;171(12):1278-86.
- Johnston JN, Campbell D, Caruncho HJ, Henter ID, Ballard ED, Zarate CA. Suicide Biomarkers to Predict Risk, Classify Diagnostic Subtypes, and Identify Novel Therapeutic Targets: 5 Years of Promising Research. *Int J Neuropsychopharmacol*. 2022;25(3):197-214.
- Wisłowska-Stanek A, Kołosowska K, Maciejak P. Neurobiological Basis of Increased Risk for Suicidal Behaviour. *Cells*. 2021;10(10):2519.
- Arvind BA, Gururaj G, Loganathan S, et al. Prevalence and socioeconomic impact of depressive disorders in India: multisite population-based cross-sectional study. *BMJ Open*. 2019;9(6):e027250.
- Singh OP. Startling suicide statistics in India: Time for urgent action. *Indian J Psychiatry*. 2022;64(5):431-432.
- Mudgal V, Pal V, Rastogi P, Lohokare R. A comparative study of inflammatory marker highly sensitive C-reactive protein in depression patients exhibiting suicidal behaviour and depression patients without suicidal behaviour. *Int J Res Med Sci*. 2020;8:1086-93.
- Rane A, Nadkarni A. Suicide in India: a systematic review. *Shanghai Arch Psychiatry*. 2014;26(2):69-80.
- Singh M, Shekhar C, Shri N. Patterns in age at first marriage and its determinants in India: A historical perspective of last 30 years (1992-2021). *SSM Popul Health*. 2023;22:101363.
- Jefferis BJ, Nazareth I, Marston L, et al. Associations between unemployment and major depressive disorder: evidence from an international, prospective study (the predict cohort). *Soc Sci Med*. 2011;73(11):1627-1634.
- Rohan KJ, Rough JN, Evans M, et al. A protocol for the Hamilton Rating Scale for Depression: Item scoring rules, Rater training, and outcome accuracy with data on its application in a clinical trial. *J Affect Disord*. 2016;200:111-118.

30. Osman A, Bagge CL, Gutierrez PM, Konick LC, Kopper BA, & Barrios FX. The Suicidal Behaviors Questionnaire-Revised (SBQ-R): Validation with Clinical and Nonclinical Samples. *Assessment* 2001;8(4):443-454.
31. Kirino E. Escitalopram for the management of major depressive disorder: a review of its efficacy, safety, and patient acceptability. *Patient Prefer Adherence*. 2012;6:853-861.
32. Jiang K, Li L, Wang X, et al. Efficacy and tolerability of escitalopram in treatment of major depressive disorder with anxiety symptoms: a 24-week, open-label, prospective study in Chinese population. *Neuropsychiatr Dis Treat*. 2017;13:515-526.
33. O'Brien SM, Scott LV, Dinan TG. Antidepressant therapy and C-reactive protein levels. *The British Journal of Psychiatry*. 2006 May;188(5):449-52.
34. Chavda N, Kantharia ND, Jaykaran. Effects of fluoxetine and escitalopram on C-reactive protein in patients of depression. *Journal of Pharmacology and Pharmacotherapeutics*. 2011;2(1):11-6.
35. Chung HY, Kim DH, Lee EK, et al. Redefining Chronic Inflammation in Aging and Age-Related Diseases: Proposal of the Senoinflammation Concept. *Aging Dis*. 2019;10(2):367-382.
36. Ferrucci, L., Fabbri, E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. *Nat Rev Cardiol* 15, 505–522 (2018).
37. Nehring SM, Goyal A, Patel BC. C Reactive Protein. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK441843/>
38. Janakiram C, Mehta A, Venkitachalam R. Prevalence of periodontal disease among adults in India: A systematic review and meta-analysis. *J Oral Biol Craniofac Res*. 2020;10(4):800-806.
39. Ding D, Gale J, Bauman A, Phongsavan P, Nguyen B. Effects of divorce and widowhood on subsequent health behaviours and outcomes in a sample of middle-aged and older Australian adults. *Sci Rep*. 2021;11(1):15237
40. Srivastava S, Debnath P, Shri N, Muhammad T. The association of widowhood and living alone with depression among older adults in India. *Sci Rep*. 2021;11(1):21641.
41. Aremu TO, Oluwole OE, Adeyinka KO, Schommer JC. Medication Adherence and Compliance: Recipe for Improving Patient Outcomes. *Pharmacy (Basel)*. 2022;10(5):106.
42. Ivandic I, Kamenov K, Rojas D, Cerón G, Nowak D, Sabariego C. Determinants of Work Performance in Workers with Depression and Anxiety: A Cross-Sectional Study. *Int J Environ Res Public Health*. 2017;14(5):466.
43. Rothermundt M, Arolt V, Fenker J, Gutbrodt H, Peters M, Kirchner H. Different immune patterns in melancholic and nonmelancholic major depression. *J Affect Disord* 2001;63:93-102.
44. Kenis G, Maes M. Effects of antidepressants on the production of cytokines. *Int J Neuropsychopharmacol* 2002;5:401-12.
45. Sinead M, Lucinda V, Timothy G. Antidepressant therapy and C-reactive protein levels. *Br J Psychiatry* 2006;188:449-52