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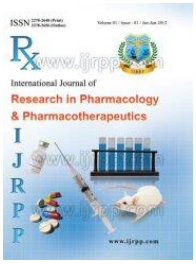

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# The effect of escitalopram on biomarkers of depression in patients of multidrug resistant tuberculosis (MDR-TB) suffering with depression

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## ABSTRACT

### Aim

To study the effect of Escitalopram on biomarkers of depression in patients of multidrug resistant tuberculosis (MDR-TB) suffering with depression.

### Material and Methods

Total 35 diagnosed MDR TB patients were selected from Tuberculosis and Respiratory diseases department complaining depression symptoms in their MDR TB treatment follow up. These patients were referred to Psychiatry OPD for diagnosis of depression.

Hamilton Depression Rating Scale (HDRS) score was computed to categorize depression as mild, moderate and severe depression. 24 MDR TB patients diagnosed with mild to moderate depression were enrolled. Escitalopram (10mg) were administered to enrolled patients already taken Standard MDR-tuberculosis treatment. Follow up was done at day 30 and day 120.

Depression improvement assessed by HDRS score and biomarker alterations assessed by serum lipid profile- Serum cholesterol, Triglyceride (Tg), Low density lipoprotein (LDL), High density lipoprotein (HDL) and very low density lipoprotein cholesterol (VLDL). Data were compiled and analyzed using SPSS 20.0 and paired t – test.

### Result

Total 19 patients had completed the study. 3 and 2 patients were lost in follow up at day 30 and 120 respectively. Baseline HDRS score (13.53 ± 2.58) were decreased at day 30 (6.11 ± 1.28) and Day 120 (3.05 ± 0.91) which were significant ($p<0.001$). Lipid profile parameters were not increased significantly at any follow up.

**Conclusion**

Escitalopram drug therapy improved depression symptoms without significantly affecting the biomarkers for depression (lipid profile).

**Keywords:** Escitalopram, Serum cholesterol, Triglyceride, Low density lipoprotein, High density lipoprotein

## INTRODUCTION

Multidrug resistant tuberculosis (MDR-TB) is a challenging task for health care providers to control tuberculosis. According to the WHO Global TB Report- 2016, TB remained one of the top 10 causes of death worldwide. There were an estimated 480 000 new cases of MDR-TB and India, China and the Russian Federation accounted for 45% of these cases [1]. An estimated 1.3 lakh incident multi-drug resistant TB patients emerge annually in India which included 79000 MDR-TB Patients out of the notified pulmonary cases [2].

The psychological aspects of tuberculosis have always been a topic of interest over the centuries and the association of tuberculosis with mental illness became a subject of statistical analysis as early as 1863 [3]. Psychiatric complications like depression, anxiety, and psychosis, can greatly influence the quality of life of these patients, as well as physicians' attitudes toward MDR-tuberculosis therapy [3]. It is estimated that 20% of patients with somatic disease suffer from major depression. [4]. Reported rate of depression in MDR-TB varies from 6.2% to 22%. [5]

Drugs like Cycloserine (Cs), fluoroquinolones, Isoniazid (H), Ethionamide (Eto) /Prothionamide (Pto) can cause depression in these patients as a adverse effect of these drugs and if depression is more significant, then antidepressant therapy is initiated which included Tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) [6]. Escitalopram, the *S*-enantiomer of Citalopram, is the newest marketed SSRI, introduced in 2002 [7]. It selectively binds to the human serotonin transporter (SERT), and inhibits serotonin (5-HT) reuptake and increases the amount of serotonin in synaptic clefts, which results in its antidepressant action [8].

Lipid-induced changes in brain chemistry affect the lipid environment of the brain and modulate neurotransmitter action and function of neuronal proteins [9]. The tertiary and quaternary structures of neuronal proteins as receptors, ion channels and protein kinases depend upon the electrical and fluidity parameters determined by electrolytes and the lipid environment of the brain [9]. Lipid and electrolyte abnormalities have a marked impact on neuronal disturbance and ultimately lead to mood and behavioral problems [9]. Serum Lipids may be used as peripheral biomarkers that can be used for diagnosis, monitoring response to treatment and patient stratification [10]. The levels of serum cholesterol and cholesterol-containing molecules like LDL, HDL have been linked to Major depressive disorder (MDD). Decreases in total serum cholesterol are commonly observed in depressed patients suffering from MDD when compared to healthy controls [11]. Several studies have been performed to establish a relationship between cholesterol levels and depression. Majority of the studies have concluded that low cholesterol levels are associated with depression and suicide [12].

Several studies have been done to evaluate the clinical effectiveness of antidepressant drugs in depressed patients but no study has been done to observe the effect of antidepressant drugs on biomarker alterations in MDR TB patients. Therefore present study has been planned to know the effect of Escitalopram (antidepressant drug) on clinical improvement and biomarker (lipid profile) alteration in MDR TB patients suffering with depression.

## MATERIAL AND METHODS

Total 35 diagnosed MDR TB patients were selected from Out- patients department (O.P.D.) and in- patients department (I.P.D.) of Tuberculosis and Respiratory diseases during the study period of 12 months complaining depression symptoms. These patients then referred to Psychiatry OPD for diagnosis of depression and Hamilton Depression Rating Scale score was computed to categorized depression as mild, moderate and severe depression. 24 MDR TB patients diagnosed with depression who had category of mild to moderate depression were enrolled. Before enrollment written informed consent was taken. Institutional Ethics Committee approval was taken before start of study.

### Inclusion criteria

1. All male and female patients between age group of 15 to 65 years.
2. Patients of MDR-TB (MDR TB Confirmed by Cartridge based nucleic acid amplification test )
3. Patients with mild to moderate depression (diagnosed as depressed by International classification of diseases, tenth revision, diagnostic criteria for research ICD-10 DCR)

### Exclusion Criteria

1. Patients of severe depression.
2. Patients of depression with suicidal tendency.
3. Patients taking antidepressant drug before enrolment
4. Patients taking any drug other than the prescribed during study
5. HIV & Hepatitis B positive cases
6. Pregnant females
7. Patients of MDR-TB with psychiatric illness other than mild to moderate depression.
8. Patients with diabetes, hypertension, renal impairment and abnormal liver function test.
9. Patients not willing to participate in the study.

Escitalopram (10mg) in the form of single oral tablets were administered to enrolled patients already taken Standard MDR-tuberculosis treatment. Follow up was done at day 30 and day 120. Hamilton depression rating scale score was computed for depression improvement and for change in biomarker of depression, serum lipid profile (Serum cholesterol, Triglyceride, High density lipoprotein cholesterol, Low density lipoprotein cholesterol and Very low density lipoprotein cholesterol) were done at every follow up.

### Data management and statistical analysis

Data were compiled and analyzed using SPSS 20.0. Data were analyzed using Mean, Standard Deviation (SD). Paired t – test was used for statistical analysis. p value <0.05 was considered as significant.

## RESULTS

Total 24 diagnosed mild to moderate depressed patients were included in the study. These patients were prescribed Escitalopram (10mg/day) single oral tablet. Total 19 patients had completed the study. 3 and 2 patients were lost in follow up at day 30 and day 120 respectively.

### Patients Baseline data

The numbers of males patients were 13 (68.42%) and females were 6 (33.33%). The mean (± SD) age were 30 (± 13). Mild depressed patients (HDRS Score 8-13) were 9 (47.36%) and moderate depressed (HDRS Score 14-18) were 10 (52.63%). The mean (± SD) of lipid profile parameters were serum cholesterol 146.37± 18.64, serum triglyceride (Tg) 75.44± 17.41, serum high density lipoprotein cholesterol (HDLc) 42.88± 09.29, serum low density lipoprotein cholesterol (LDLc) 48.89± 17.44 and serum very low density cholesterol (VLDL) 20.79± 04.29. At baseline HDRS score mean (± SD) was 13.53 ± 2.58.

### Effect of Escitalopram on depression

At base line, mean (± SD) HDRS score were 13.53(±2.58). At day 30 and day 120 after initiation of Escitalopram drug therapy the mean (± SD) HDRS scores were 6.11 ± 1.28 and 3.05 ± 0.91 respectively. **(Table 1) and (Figure 1)** from these observations it was inferred that there were decrease in HDRS score from the day 0 (base line) to each follow-up at day 30 and day 120 and the mean decrease in HDRS scores were significant ($p<0.001$) at each follow-up.

**Table 1: Change in HDRS score after Escitalopram drug therapy**

| Escitalopram (10mg/day) (n=19) | | | |
|---|---|---|---|
| **HDRS Score (Mean ±SD) At day '0'** | **Follow up** | **Change in HDRS Score (Mean ±SD) at follow up** | **$p^*$ value** |
| 13.53 ± 2.58 | At day '30' | 6.11 ± 1.28 | < 0.001 significant |
| 13.53 ± 2.58 | At day '120' | 3.05 ± 0.91 | < 0.001 significant |

**($p^*$ < 0.05 is significant)**

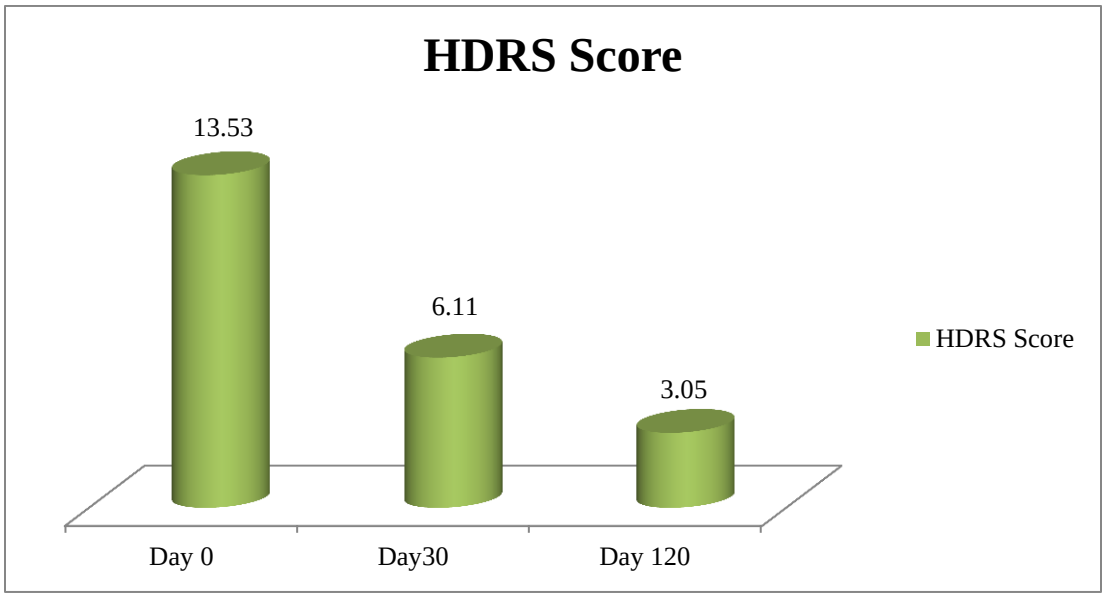


**Figure 1: Change in HDRS score after initiation of Escitalopram drug therapy**

## Effect of Escitalopram on biomarkers (lipid profile)

At base line, the mean (± SD) Serum cholesterol was 146.37 ± 18.64; Tg was 75.44 ± 17.41; HDLc was 42.88 ± 09.29; LDLc was 48.89± 17.44 and VLDL was 22.79 ± 04.29.At day 30 the mean (± SD) serum cholesterol level was 146.94± 17.26; Tg was 75.78 ± 19.16; HDLc was 43.58 ± 05.27; LDLc was 50.5 ± 12.08; VLDL was 21.14 ± 02.58 and at day 120 the mean (± SD) serum cholesterol level was 147.05± 17.25; Tg was 76.47 ± 15.60; HDLc was 44.68 ±06.64; LDLc was 50.00 ± 11.42 and VLDL was 22.10 ± 02.73 **.** There were no significant increase (p> 0.05) in Serum Cholesterol ;Tg; HDLc; LDLc and VLDL cholesterole levels from base line to the followup at day 30 and day 120. **(Table 2) and (Figure 2).**

**Table-2 Change in serum lipid profile after initiation of Escitalopram**

| ( Escitalopram) (n=19) | | | |
|---|---|---|---|
| **Lipid Profile Level (Mean ± SD)** | **Day '0'** | **Day '30'** | **$p^*$ value** |
| **Serum cholesterol (mg/dl)** | 146.37 ±18.64 | 146.94 ± 17.26 | 0.225 |
| **Serum triglyceride (mg/dl)** | 75.44 ± 17.41 | 75.78 ±19.16 | 0.826 |
| **Serum HDL Cholesterol (mg/dl)** | 42.88 ± 09.29 | 43.58 ± 05.27 | 0.708 |
| **Serum LDL Cholesterol (mg/dl)** | 48.89 ± 17.44 | 50.5 ± 12.08 | 0.678 |
| **Serum VLDL Cholesterol (mg/dl)** | 20.79 ± 04.29 | 21.14 ± 02.58 | 0.657 |

| | Day '0' | Day '120' | p* value |
|---|---|---|---|
| **Serum cholesterol (mg/dl)** | 146.37 ±18.64 | 147.05 ± 17.25 | 0.243 |
| **Serum triglyceride (mg/dl)** | 75.44 ± 17.41 | 76.47 ± 15.60 | 0.192 |
| **Serum HDL cholesterol (mg/dl)** | 42.88 ± 09.29 | 44.68 ± 06.64 | 0.935 |
| **Serum LDL cholesterol (mg/dl)** | 48.89 ± 17.44 | 50.00 ± 11.42 | 0.653 |
| **Serum VLDL cholesterol (mg/dl)** | 20.79 ± 04.29 | 22.10 ± 02.73 | 0.195 |

**p* value < 0.05 is significant**

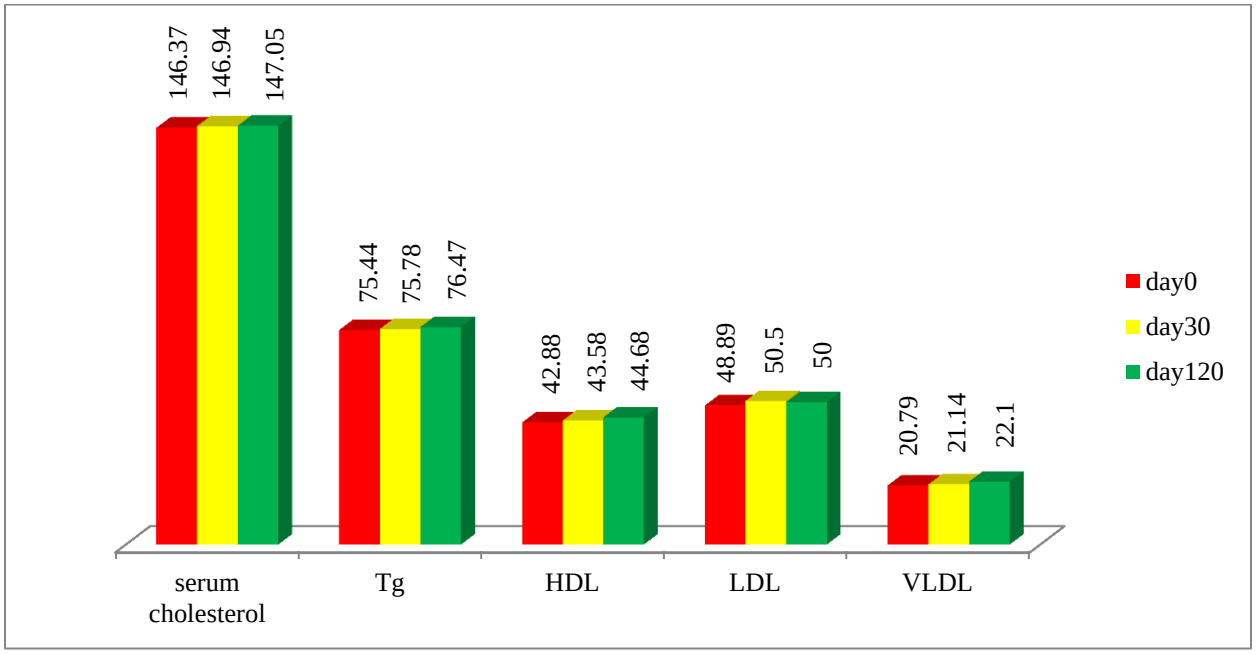


**Figure 2:Change in Mean serum lipid profile levels after initiation of Escitalopram**

## DISCUSSION

The present study simultaneously analyzed the effect of Escitalopram on biomarker (Lipid profile) alterations and depression symptoms improvement. After Escitalopram drug administration the HDRS score were decreased significantly at day 30 and day 120 from baseline. The lipid profile parameters were not increased significantly after administration of Escitalopram drug therapy.

In our study after administration of Escitalopram drug therapy the HDRS score at day 30 was 6.11 ± 1.28 and at day 120 was 3.05 ± 0.91 ,which showed significantly decrease ($p< 0.001$) in HDRS score from baseline ( HDRS score 13.53 ± 2.58); whereas lipid profile parameters serum cholesterol at day 30 and day 120 was 146.94 ± 17.26 and 147.05 ± 17.25, Tg was 75.78 ±19.16 and 76.47 ± 15.60, HDL-C was 43.58 ± 05.27 and 44.68 ± 06.64, LDL-C was 50.5 ± 12.08 and 50.00 ± 11.42 and VLDL-C was 21.14 ± 02.58 and 22.10 ± 02.73,which showed no significant increase from baseline. Deisenhammer et al. [13] (2004) had done a study on serum lipid profile and measured serum cholesterol in 92 patients after 1 week and 4 weeks of antidepressant treatment and found that neither a significant change in serum cholesterol levels nor a correlation between cholesterol levels and clinical improvement was found. Our study showed similar results with this study but there was difference in number of patients, duration of study, antidepressant drug and lipid profile parameters.

In another 6 month experimental study done by Ashique Ali Arain et al [14] (2017) on Escitalopram, 72 diagnosed patients of depression were analyzed for total cholesterol, HDL, LDL and Triglycerides before intervention. 8 patients were dropped out from study as they lost follow up after 1 month. Same test were repeated in 64 patients who completed the study. After 6 weeks there were significant reduction in total cholesterol, LDL and Triglyceride when compared with the pretreatment values and there was

no significant difference in HDL levels before and after treatment. In our study the mean change in lipid profile parameters after initiation of Escitalopram showed that there were increased in all lipid profile parameter levels but this increase was not significant. Our study was not in accordance with this study because of small sample size and long duration of study.

Another study done by Ozlem O. Eker et al. [15] (2017) on depressive patients included 35 females and 5 men patients and 32 healthy controls. These patients had received antidepressant treatment (Sertraline, Escitalopram, Fluoxetine, and Venlafaxine) for 8 weeks. Body measurements were performed, and lipid, fasting blood glucose, and insulin levels were measured before and after treatment in patients and once in healthy controls. Insulin resistance was evaluated using the homeostasis model assessment (HOMA) index. After antidepressant treatment it was observed that there were increase in serum cholesterol and high density lipoprotein (HDL) cholesterol levels in Escitalopram group whereas in patients treated with Sertraline there was no change in Body mass and lipid levels. Our study differed from this study that the significant increased levels were not observed in any lipid profile parameters and this may be because of less no. of female patients and small sample size.

Another prospective study using SSRI was carried out by Murat Beyazyüz et al. [16] (2013) to investigate metabolic syndrome abnormalities caused by SSRIs in generalized anxiety disorder, Ninety-seven female patients aged 20-41 years without any metabolic or psychiatric co-morbidity were included in the study. Fluoxetine, Sertraline, Paroxetine, Citalopram and Escitalopram were randomly given to the patients. Metabolic parameters including BMI, waist circumference and the levels of fasting glucose, total cholesterol, triglyceride, HDL, LDL and blood pressure were measured before and after 16 weeks of treatment. Patients were controlled for their food intake in terms of continuation of their usual eating habits during study. Blood samples were taken before and after sixteen weeks of treatment and there were significant increase in the levels of triglyceride in Escitalopram group. Our study differed from this observation that the increased levels of triglyceride were not significant. The other parameters of lipid profile were also increased but the change was not significant. Our study differed from this study in the aspects that we included both male and female patients with depression, small sample size and age distribution.

## CONCLUSION

The present clinical study was conducted to observe the effect of Escitalopram on biomarkers of depression (lipid profile) in patients of multidrug resistant tuberculosis suffering with depression. The inference reveled that as the depression symptoms improved following Escitalopram drug therapy, the biomarkers of depression (lipid profile parameters) were not significantly increased from baseline. Therefore it seems to improve the depression symptoms without significantly affecting the biomarkers of depression. It is emphasized to conduct similar studies with large sample size to explore the more reliable outcomes as our study has various limitations like small sample size, short duration and mild to moderate depressive patients.

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