DOI: 10.7860/NJLM/2022/55879.2666

Original Article

Pharmacology Section

Evaluation of Metabolic Effects of Antidepressant Drugs in Patients with Mood Disorders: A Case-control Study

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ABSTRACT

Introduction: Treatment of mood disorders like Major Depressive Disorder (MDD) and anxiety etc., includes long-term use of antidepressants which alleviate the symptoms with proven efficacy and safety. Metabolic syndrome is a cluster of disorder which includes body weight gain, abdominal obesity, hypertriglyceridaemia, hypertension, and hyperglycaemia either individually or collectively. The link between metabolic adverse effects of antidepressants usage requires further elaboration.

Aim: To evaluate the metabolic adverse effects of antidepressant drugs among the patients with mood disorders and also to compare with healthy controls.

Materials and Methods: This case-control study was conducted in the Department of Pharmacology and Department of Psychiatry at a tertiary care teaching hospital, Puducherry, India from January 2018 to June 2018. A total of 66 participants following the inclusion criteria, were divided into two groups- group A: 33 age and sex matched healthy subjects were enrolled as control group and group B: 33 patients diagnosed to have MDD, anxiety and other mood disorders were the drug treated group. Metabolic profile was screened by body weight, Body Mass Index (BMI), Waist Circumference (WC), Fasting Blood Sugar (FBS) and lipid profile. Independent Student's t-test was used to compare the lipid profile among groups and one way Analysis of Variance (ANOVA) followed by Dunnet's t test was used to compare demographic data and lipid profile.

Results: The mean age of the study participants was 42.0±13.0 years and 41.3±14.9 years in group A and group B respectively. In present study, male 38 (57.6%) outnumbered females 28 (42.4%). BMI in the groups A and B was 27.0±3.0 kg/m^2 and 29.4±0.9 kg/m^2 respectively (p-value <0.05). No differences were observed with height, weight and WC between the groups. FBS level was significantly increased in group B 114.6±13.8 (mg/dL) as compared to group A, 93.2±4.8 (mg/dL). No significant changes was observed for renal parameters, blood pressure and complete blood count except lymphocyte count (p-value=0.015) between the groups. The serum High Density Lipoprotein (HDL) was increased in group B as compared to group A but the increase was within the normal range. Statistically significant increase in Low Density Lipoprotein (LDL) and total cholesterol was seen in group B when compared to group A.

Conclusion: The present study elucidated the increase in the BMI, FBS, serum LDL and total cholesterol in the antidepressant treated group when compared with control group.

Keywords: Body mass index, Fasting blood glucose, Lipid profile, Waist circumference

INTRODUCTION

Mood disorder is the most common psychiatric disorder affecting people of all ages [1,2]. This disability is usually recurrent or long lasting, commonly linked to medical morbidity and mortality [2]. According to World Health Organisation (WHO), Major Depressive Disorder (MDD) affects 280 million people approximately in the world contributing to global burden [3]. This devastating illness affects 350 million people worldwide reducing the quality of life of the individuals with various impacts on behavioural changes and social factors [4]. Annually 5.8% of men and 9.5% of women experience episodes of depression, which is projected by suicidal behaviour, ideation, completions, attempts and accounts for 60% of suicidal deaths every year [5].

The mortality rates of patients with this deteriorating illness are 2-3 times higher than the normal population and their life expectancy is also reduced [5]. They usually maintain an unhealthy lifestyle choice which leads to poorer physical outcomes [6]. Depression is manifested by mental symptoms like feeling of sadness, thought of guilty, worthlessness, anxiety, emptiness, irritability, restlessness, problems with concentration, loss of interest and pleasure (anhedonia). The physical symptoms includes aches, fatigue, disturbance in appetite, sleep, deficits in cognition and energy with effects on the human health and overall functioning to a great extent [7,8].

Management of depression and anxiety includes long-term use of antidepressants which alleviate the symptoms with proven efficacy and safety. Different class of antidepressants like tricyclic antidepressants, monoamine oxidase inhibitors, Selective Serotonin Reuptake Inhibitor (SSRIs), Selective Serotonin Norepinephrine Reuptake Inhibitor (SNRIs) and atypical antidepressants are available each with specific mechanism of action [8]. New class of antidepressants has emerged considerably since the discovery of the "first-generation" antidepressants (tricyclic and monoamine oxidase inhibitors) introduced in 1950s. Compared with conventional antidepressant drugs, newer drug classes have improved tolerability and a higher level of efficacy. Especially the discovery of SSRIs (5-hydroxytryptamine, 5-HT) has grown as a major therapeutic advance in treating depression and marked a milestone in psychopharmacology.

In addition to being established treatments of depression, SSRIs have well-documented efficacy in the anxiety disorders, panic disorders, Obsessive Compulsive Disorder (OCD), dysthymic disorder, premenstrual syndrome, bipolar disorder, depression and bulimia nervosa. The abundance of biological substrates, receptors and neuro-anatomical pathways for 5-HT are the candidates to mediate not only the therapeutic actions of SSRIs but also the side-effects [8]. Metabolic syndrome is a cluster of disorder which includes body weight gain, abdominal obesity, hypertriglyceridaemia, hypertension, and hyperglycaemia either individually or collectively. This predisposes to risk of coronary artery disease and diabetes mellitus in adults and adolescents [9]. Patients treated with antidepressants may

be predisposed to metabolic adverse effects which are triggered by limited access to healthcare; drug induced pharmacological effects, poor diet, substance abuse and sedentary lifestyle [9]. Weight gain, increase in WC, sexual dysfunction, drug interaction, discontinuation symptoms and extra-pyramidal symptoms are found in these patients which are also genetically determined [10]. Use of antidepressants has also been associated with increased risk of dyslipidaemia, type 2 diabetes mellitus and other metabolic adverse effects [11]. Based on these evidences, the association between metabolic effects and use of antidepressants was found to be multifaceted and require further elaboration. Studies done in this context was observed from the North India [12,13]. Hence, present study was conduced to evaluate the metabolic effects in patients who were treated with antidepressants among the South Indian population and also to compare with healthy controls.

MATERIALS AND METHODS

This case-control study was conducted in Department of Pharmacology and Department of Psychiatry at a tertiary care teaching hospital, Pondicherry, India for a period of six months (January 2018 to June 2018). The study was commenced after getting permission from the Institutional Ethics Committee (IEC) (SVMCH/IEC2017-Oct/24). Written informed consent was taken from all the participants. Confidentiality was maintained throughout the study.

Inclusion criteria: Patients aged between 20 to 65 years, irrespective of gender, who were a known case of depression, anxiety and other mood disorders based on Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) criteria [14] and were treated with antidepressant drugs for a minimum of six months duration were included. Age and sex matched healthy controls were also included.

Exclusion criteria: Patients with previous history of metabolic and endocrine disorders like hyperlipidaemia, diabetes mellitus, thyroid disease and patients on antidiabetic, hypolipidaemic therapy, antiepileptic, antipsychotic, antiparkinson drugs, birth control pills, steroids, propranolol, thiazide diuretics and agents that induce weight loss, patients with bipolar disorder receiving mood stabilisers, with eating disorder, with history of alcoholism, substance abuse and pregnant and lactating females were excluded from the study.

Sample size calculation: Sample size was calculated based on the previous study [4], considering total cholesterol value of 150 mg/dL, alpha error of 5% and beta error of 20% the sample size was calculated as 33 in each group. A total of 66 participants satisfying the selection criteria were enrolled and divided in two groups:

Group A (Control group): Included 33 age and sex matched healthy controls.

Group B (Drug treated group-Cases): Included 33 patients treated with antidepressants for minimum of six months duration.

The study procedure and their role in this study were fully explained to the controls (group A) and cases (group B).

Data Collection Tools

A specially designed proforma was used to record the data. Demographic data like age, gender, residential address, occupation and socio-economic status was assessed using modified BG Prasad scale [15]. Metabolic profile was evaluated by screening patient's body weight, height, BMI, WC, FBS, lipid profile {LDL, HDL, Very Low Density Lipoprotein (VLDL), Triglycerides (TG), Total Cholesterol (TC)} and blood pressure. Complete blood count and renal parameters (blood urea, serum creatinine) were also assessed. Any adverse drug reaction during the study period was reported.

Body weight was measured using standardised weighing machine in kilogram unit. Height was calculated using height ruler in centimeters by making the subject stand with shoes off, feet together and arms by the side. BMI was calculated by the formula; weight in kilogram by height in meter square (BMI=weight in kilogram/height in meter^2). The WC was measured at the level of umbilicus and upper limit of the iliac crest, without applying pressure which would change the result. The patient was made to stand and freely breathing with the waist area uncovered. Blood pressure measurement was done in sitting position, after atleast five minutes of rest using a standard sphygmomanometer and a stethoscope.

Fasting blood samples were collected in the morning between 7 a.m. and 8 a.m. by venipuncture of antecubital vein with all aseptic precautions. Five mL of blood was withdrawn using a dry disposable syringe under sterile conditions in a sterile plain vial and sent to the laboratory immediately. Serum was separated by centrifugation at 3000 rpm for 15 minutes. Fresh serum was used for estimation of TC, TG, VLDL, LDL and HDL-c. The tests were carried out in an automated clinical autoanalyser. FBS was estimated using glucose diagnostic reagent kit (manufactured by Trans Asia Bio-Medicals Ltd. India in technical collaboration with Erba diagnostics Manheim GmbH, Germany) and tabulated below in [Table/Fig-1]. Complete Blood Count (CBC) was performed with 2 mL venous blood collected in heparinised tubes and determined using autoanalyser (Dia- CHEM 300 plus) [Table/Fig-1] [16,17].

Parameters	Method	Reference range
Fasting blood glucose	GOD- POD	80-100 mg/dL
Serum TC	CHOD-POD	125-200 mg/dL
Serum TG	GPO-TRINDER	<150 mg/dL
Serum HDL-C	Cholesterol oxidase-peroxidase	>40 mg/dL
Serum VLDL-C	Friedewald's equation	<30 mg/dL
Serum LDL-C	Friedewald's equation	<100 mg/dL
Blood urea	GLDH	15-40 mg/dL
Serum creatinine	Jaffe's	0.6-1.1 mg/dL
Haemoglobin	Autoanalyser	12-15 mg/dL
Total leukocytes count	,,	4500-11000 cell/cu.mm
Neutrophils	,,	40-65%
Lymphocytes	,,	30-50%
Eosinophils	,,	2-8%
Basophils	,,	<1%
Erythrocyte sedimentation rate	,,	5-20 mm/hr

[Table/Fig-1]: Levels of biochemical and haematological parameters (Normal reference values).
GOD-POD: Glucose oxidase peroxidase; CHOD-POD: Cholesterol oxidase peroxidase; GLDH: Glutamate dehydrogenase; GPO: Glycerol phosphate oxidase

STATISTICAL ANALYSIS

Data was entered and analysis was done using Statistical Package for the Social Sciences (SPSS) software 23.0 for Windows (Chicago, Illinois, USA). Frequencies with percentages were calculated for categorical variables and mean±standard deviation were calculated for continuous variables. Independent Student's t-test (2 tailed) was used to compare the lipid profile and blood parameters between the groups. One way Analysis of Variance (ANOVA) followed by Dunnet's t-test was used to compare different antidepressant drugs with demographic data and lipid profile. The p-value <0.05 was considered statistically significant.

RESULTS

The mean age of the study participants were 42.0±13.0 years and 41.3±14.9 years in group A and group B, respectively. In present study, males 38 (57.6%) outnumbered females 28 (42.4%) (p-value <0.05). BMI was more (29.4±0.9 kg/m^2) in group B when compared to group A (27.0±3.0 kg/m^2) (p<0.05). Maximum number of patients in group B 13 (39.4%) and in group A 12 (36.4%) were middle class. Patients treated with antidepressants between 6 months to 1 year was

found to be higher 19 (57.6%) than the others. Socio-demographic and other clinical characteristics are shown in [Table/Fig-2].

Characteristics	Group A (n=33) (Mean±SD)	Group B (n=33) (Mean±SD)	p-value
Age (years)	42.0±13.0	41.3±14.9	0.841
Height (cms)	160.4±5.8	159.2±6.2	0.421
Weight (kg)	70.6±9.4	74.6±13.8	0.173
Waist circumference (cms)	96.7±7.5	97.6±10.8	0.061
BMI (kg/m^2)	27.0±3.0	29.4±0.9	0.05*
SBP (mmHg)	119.0±5.2	120.7±10.1	0.396
DBP (mmHg)	80.3±4.6	80.0±6.6	0.830
Socio-economic status n (%)			
Lower	2 (6.1)	4 (12.1)	0.01*
Lower middle	4 (12.1)	9 (27.3)	0.01*
Middle	12 (36.4)	13 (39.4)	0.1
Upper middle	11 (33.3)	5 (15.1)	0.01*
Upper	4 (12.1)	2 (6.1)	0.01*
Duration of disease (n=33) n (%)			
>6 months-1 year	-	19 (57.6)	
1-3 years	-	10 (30.3)	
3-5 years	-	4 (12.1)	

[Table/Fig-2]: Socio-demographic data and clinical characteristics of the study participants.
Independent student t-test (2 tailed); *p<0.05 was statistically significant; BMI: body mass index; SBP: Systolic blood pressure; DBP: diastolic blood pressure

The complete blood count including Haemoglobin (Hb) (gms%), total leukocytes count (cells/mm^3), erythrocyte sedimentation rate (mm/hr) and differential leukocytes count were analysed. There was a significant decrease in lymphocyte count in group B (31.7±7.3%) when compared to group A (35.5±4.8%) (p-value=0.015). No significant difference was found for Hb, TLC, neutrophils, eosinophils, monocytes and basophils (p-value >0.05) [Table/Fig-3].

Complete blood count	Group A (Mean±SD)	Group B (Mean±SD)	p-value
Hb (gms%)	12.2±1.2	11.6±1.7	0.139
TLC (cells/mm^3)	9739.3±1062.9	9369.6±1587.7	0.271
ESR (mm/hr)	27.6±6.7	23.9±9.2	0.070
Neutrophils (%)	57.4±5.3	61.0±8.4	0.42
Eosinophils (%)	4.3±1.5	4.5±2.2	0.752
Lymphocytes (%)	35.5±4.8	31.7±7.3	0.015*
Monocytes (%)	3.1±6.7	2.2±1.5	0.455
Basophils (%)	0.3±0.7	0.1±0.3	0.135

[Table/Fig-3]: Comparison of complete blood count among the groups.
Values are expressed in Mean±SD; Independent student t-test (2 tailed); Hb: Haemoglobin; TLC: Total leukocytes count; ESR: Erythrocyte sedimentation rate; *p<0.05 was statistically significant

Assessment of mean FBS showed a statistically significant increase in fasting blood sugar in group B (114.6±13.8 mg/dL) when compared to group A (93.2±4.8 mg/dL) (p-value <0.0001). There was no significant change in the renal parameters such as urea and creatinine among the study participants. Comparison of lipid profile among the groups showed that there was a statistical significant increase in total cholesterol levels (214.0±51.0 mg/dL vs 165.3±21.9 mg/dL), LDL levels (124.6±49.7 mg/dL vs 90.5±19.2 mg/dL) and HDL levels (55.4±17.5 mg/dL vs 45.5±6.1 mg/dL) in group B when compared to group A (p-value=0.0001, 0.01 and 0.03), respectively [Table/Fig-4].

Among the antidepressants usage escitalopram was used by 23 (69.7%) whereas fluvoxamine and fluoxetine usage was by 5 (15.2%) subjects each. No statistical significance was observed for the age, WC, BMI, FBS and renal parameters as shown in the between the three drug treated groups [Table/Fig-5].

Parameters	Group A (Mean±SD)	Group B (Mean±SD)	p-value
FBS (mg/dL)	93.2±4.8	114.6±13.8	<0.0001**
Blood urea (mg/dL)	29.0±6.0	26.4±5.1	0.069
Serum creatinine (mg/dL)	0.7±0.1	0.8±0.1	0.127
HDL (mg/dL)	45.5±6.1	55.4±17.5	0.03*
LDL (mg/dL)	90.5±19.2	124.6±49.7	0.01*
VLDL (mg/dL)	29.3±5.5	33.7±13.3	0.081
Triglycerides (mg/dL)	148.7±28.1	168.1±61.4	0.105
Total cholesterol (mg/dL)	165.3±21.9	214.0±51.0	0.0001**

[Table/Fig-4]: Comparison of fasting blood sugar, renal parameters and lipid profile among the groups.
Analysis was done by Independent student t-test (2 tailed); *p<0.05 was statistically significant

Parameters	Drugs			p-value
	Escitalopram (Mean±SD)	Fluvoxamine (Mean±SD)	Fluoxetine (Mean±SD)	
Age (years)	39.2±13.9	53.4±12.4	38.6±18.7	0.145
WC (cm)	96.6±11.2	98.4±11.8	102±8.8	0.609
BMI (kg/m^2)	29.1±5.2	29.8±6.7	30.5±5.8	0.858
FBS (mg/dL)	114.7±13.7	108.4±12.7	120.2±15.9	0.416
Blood urea (mg/dL)	26.5±4.6	26±5.9	26.6±7.4	0.978
Serum creatinine (mg/dL)	0.7±0.1	0.6±0.08	0.9±0.2	0.135

[Table/Fig-5]: Comparison of drugs in relation to socio-demographic data and blood parameters.
Analysis was done by one way ANOVA followed by Dunnet's t-test; WC: Waist circumference; BMI: Body mass index; FBS: Fasting blood sugar

No statistical significantt difference was seen among the lipid profile (HDL, LDL, VLDL, TC, TG) of treatment groups with different antidepressants treated groups as shown in [Table/Fig-6]. No adverse drug reactions were noted during the study period.

Lipid profile	Antidepressant drugs			p-value
	Escitalopram (Mean±SD)	Fluvoxamine (Mean±SD)	Fluoxetine (Mean±SD)	
LDL (mg/dL)	116.7±54.0	167.0±23.4	118.8±23.6	0.710
HDL (mg/dL)	56.1±17.3	48.2±11.7	59.6±23.9	0.933
VLDL (mg/dL)	32.1±10.75	43.4±25.0	31.6±4.2	0.909
TG (mg/dL)	161.3±53.6	208.4±107.1	159.4±22.3	0.938
TC (mg/dL)	205.6±55.1	256.6±27.9	210±24.7	0.866

[Table/Fig-6]: Comparison of lipid profile with different antidepressants.
One way ANOVA followed by Dunnet's t test; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; TG: Triglycerides; TC: Total cholesterol

DISCUSSION

Antidepressant medication used for psychiatry disorders are associated with important metabolic adverse effects causing significant physical impairment and adverse health outcomes like type 2 diabetes and cardiovascular morbidity and mortality [18,19]. These metabolic effects were assessed by FBS, complete blood count, renal parameters and lipid profile in the present study among the antidepressant drug treated patients. The commonly used antidepressants among the drug treated group (group B) were SSRIs such as escitalopram, fluoxetine and fluvoxamine. There was statistically significant elevation of BMI among the patients treated with antidepressants when compared to the control participants. However, the use of SSRIs was not significantly associated with increase in weight and waist circumference. It was observed that present findings were supported by Demirci O et al., who studied the metabolic parameters in patients treated with citalopram showed, significant increase in the body weight, BMI and WC [20]. In contrast, significant reduction in body weight, BMI and WC was observed by Beyazyuz M et al., with fluoxetine therapy and significant increase in BMI with paroxetine therapy [21].

This study surprisingly showed that the control group BMI was also towards the overweight category (BMI-25 to 29.9 kg/m^2). Comparison of metabolic adverse effects of mirtazapine which is a noradrenergic and specific serotonergic drug with paroxetine showed that paroxetine had less association with the increase in weight and BMI in another study conducted by Munish K et al., [4]. Increase in BMI could be attributed to altered appetite, sleep, weight gain and physical activity which predisposes to metabolic syndrome [22]. No significant change in blood pressure among the study groups which was in concordant with previous study [21]. However, blood pressure change was observed with Citalopram therapy by Demirci O et al., [20].

Statistically significant changes were found in serum lipid profile among the antidepressant treated group when compared to controls. Serum HDL levels (p-value <0.05) were increased in the antidepressants treated patients and was within the normal range. Rise in LDL (p-value=0.01) and TC (p-value <0.0001) and no change with TG was also observed in the drug treated group. Based on these observations, it is well-known that antidepressants worsen metabolic status by adversely affecting the lipid profile. Study conducted by Raeder MB et al., demonstrated the significant raise in TC and LDL with no significant difference in HDL and TG in antidepressants treated patients [22]. Increase in TC and HDL cholesterol levels was also observed with yet another study by Ozlem OK et al., [2]. However, significant reduction in TC, LDL, and TG with fluoxetine therapy and increase in TC, LDL and no change in HDL with paroxetine therapy was also observed in the previous study [6].

Paroxetine, citalopram and citalopram treatment groups were associated with increase in serum TG levels in previous studies [11,21]. Yet another study conducted by Christoph UC et al., confirmed that the frequency of metabolic syndrome with the usage of antidepressants [6]. The use of SSRI especially paroxetine was markedly associated with obesity with no hypercholesterolemia. In addition, use of sertraline, fluoxetine and fluvoxamine was associated with both obesity and hypercholesterolemia, whereas there was no association between citalopram and any of the metabolic abnormalities was also documented [22]. But present study showed that citalopram was associated with alteration of lipid profile. A population based study demonstrated that significant affinity to serotonin reuptake transporter with antidepressants and higher levels of LDL cholesterol [23]. In this study, the limited number of patients in the subgroups like citalopram, fluoxetine and fluvoxamine makes it difficult to draw conclusion regarding the effects of different SSRIs. The effects of different SSRIs on the lipid profile could be better studied with a homogenous group of a larger study.

It has been postulated that Sterol Regulatory Element Binding Protein (SREBP) plays an important role in cholesterol metabolism. SREBP transcription factors (SREBP1 and SREBP 2) are the important regulators of cellular cholesterol and fatty acid biosynthesis in liver and fatty tissues. Activation of SREBP transcription factors by antidepressants could contribute to weight gain and metabolic effects [21,24]. The SNPs on the ABCB1 gene have been associated in alteration of the specificity and the association of these alleles with therapeutic responses and adverse reaction of the drugs were studied by Krishnan V and Nestler EJ [25]. In the present study, significant increase in FBS levels were observed in patients when compared to control group (p-value <0.0001). This is interpreted as antidepressants use had increased the diabetes risk. However insulin assay and Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was not measured. Studies have suggested that antidepressant use was associated with increased risk of developing diabetes mellitus as well as no effects on glucose metabolism [26-28].

It is presumed that hyperglycaemia induced by antidepressants could be due to inhibition of insulin cascade, weight gain, and increased levels of cortisol due to stimulated activity of Hypothalamic Pituitary Adrenal (HPA) axis predisposing to insulin resistance. SSRIs also inhibits insulin induced tyrosine phosphorylation IR substrate 2 (IRS2) protein resulting in inhibition of insulin action. Inhibition of glucose stimulated insulin release on long-term treatment with SSRI leading to endoplasmic reticulum stress responses, apoptotic process with increased caspase 3/7 activity causing β-cell death and induction of nitric oxide synthase leading to diabetic state was also postulated [29,30]. Routine complete blood count including haemoglobin, total leukocytes count, and ESR showed no significant effect of SSRIs on these parameters. Antidepressants induced blood dyscrasias had been reported but accounts to very low as per Stubner S et al., [31]. Assessment of renal parameters viz., blood urea and serum creatinine also showed no significant changes among the treatment group. Evaluation or analysis of any drug on human metabolism is usually influenced by other co-variants. In this study it was attempted to exclude some of the co-variants namely age, gender, exposure to drugs other than antidepressants, co-morbid and other psychiatric disorders. The present study represented the antidepressant drugs treated group showed significant change in the BMI, with increase in TC, LDL and FBS levels. Further longitudinal studies are required to inquire into these areas and also the impact of antidepressant intervention on metabolic parameters in patients suffering from depression.

Limitation(s)

Though the present study highlighted the metabolic adverse effects of the antidepressants, there are some limitations which cannot be ignored. The case and control groups were allotted sufficient participants, but their numbers were less when stratified into subgroups according to the intake of drugs. Since, the commonly used SSRIs were only few in our institution, the possible effects of other SSRIs on the metabolic parameters could not be studied. In addition, insulin assay and HOMA-IR was also not measured.

CONCLUSION(S)

The present study elucidated the metabolic changes associated with the antidepressant drug therapy as shown by increase in the BMI, FBS, serum LDL and TC levels in the drug treated group with no change in the renal and other haematological parameters. Nevertheless the finding of this study is important as it is imperative to do periodic monitoring of FBS, lipid profile, BMI, WC and blood pressure levels in patient treated with antidepressants therapy to prevent future cardiovascular morbidity and mortality. Further exploration studies are needed to exemplify the effects of antidepressants on different metabolic parameters.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 02, 2022
- Manual Googling: Jun 20, 2022
- iThenticate Software: Jul 01, 2022 (13%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 23, 2022**
Date of Peer Review: **May 12, 2022**
Date of Acceptance: **Jun 25, 2022**
Date of Publishing: **Oct 01, 2022**