

## ORIGINAL ARTICLE

## Effect of Therapeutic Intervention on Salivary Alpha Amylase and Serum Lipid Profile in Major Depressive Disorder

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### ABSTRACT

Major depressive disorder is a psychosocial as well as public health burden. High salivary alpha amylase (sAA) level and dyslipidemia have been observed in few occasions among major depressive disorder (MDD) patients. A hospital based longitudinal study was conducted in the Department of Biochemistry, Burdwan Medical College & Hospital, West Bengal, India, to determine changes in salivary alpha amylase and serum lipid profile before and after therapeutic intervention in MDD patients. The study included a total of 50 major depressive disorder patients selected purposively. We included newly diagnosed drug naïve patient of MDD aged between 20 and 50 years. Exclusion criteria were: presence of serious medical illness like HIV, Cancer, CKD etc. (assessed through physical examination and routine laboratory screening), any history of drug abuse and presence of another pre- or co-existing major psychiatric disorders, e.g., schizophrenia, panic attack, post traumatic stress disorders, etc. Moreover, patients who were unwilling to participate in the study or already having anti-depressant medications or any other drugs that may cause alteration in serum lipid profile were also excluded. Drug naïve newly diagnosed MDD patients, with gradual improvement of their depressive status [assessed by HDR-S ( $p < 0.001$ ) and CGI-S ( $p < 0.001$ ) at 6 and 12 weeks both] by therapeutic interventions showed significant decrease in sAA level ( $p < 0.001$ ) and increasing and decreasing trend in HDL-C ( $p < 0.001$ ) and LDL-C ( $p < 0.01$ ) level respectively. The only significant negative correlation was found between HDL-C level and salivary alpha amylase (sAA) level ( $r = -0.291$ ;  $p < 0.05$ ) after 12 weeks of treatment. Salivary alpha amylase and serum lipid profile can be used as biochemical indicators in major depressive disorder patients.

**Keywords:** Major depressive disorder, salivary alpha amylase, lipid profile, therapeutic intervention

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### INTRODUCTION

Major depressive disorder (MDD), also known as, depression is a serious medical illness characterized by melancholic feeling of sadness or grief, which can decrease the person's ability to work, characterized by periods of repeated remission and exacerbation.<sup>1</sup> Stress response mimics similar episodes and also has same mediators like depression. Thus many of the clinical presentations of major depression also reflect unbalancing of the stress response. It also leads to loss of cognitive adaptability and

activation of sympathetic system.<sup>2</sup> The stress response of salivary alpha amylase has been suggested as an index for sympathetic nervous system activation.<sup>3</sup> Salivary alpha amylase concentration, under stressful conditions can be used as an indicator of plasma catecholamine level and may be a direct mediator of catecholamine activity. A classical surrogate marker for adrenal medullary activity is alpha amylase, which although not a hormone, shows the same excretion pattern as catecholamines.<sup>4</sup> On the other hand, depression may have an association with metabolic syndrome.<sup>5</sup> It has been characterized

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by increased waist circumference, triglyceride, blood pressure, fasting blood glucose, and low HDL-cholesterol.<sup>6,7</sup> With the increase in sedentary lifestyle, leading to obesity, the prevalence of the metabolic syndrome is estimated to further increase in coming years.

Few peripheral metabolites have been shown to be associated with mood in healthy individuals or patients with CNS disease or psychiatric disorders.<sup>8</sup> Laboratory findings have revealed that major depression is accompanied by decreased formation of cholesteryl esters and also disorder of reverse cholesterol transport. The later is reportedly accompanied by lower serum HDL-cholesterol.<sup>9</sup> Hence, we have proposed this study to determine changes in salivary alpha amylase and serum lipid profile before and after therapeutic intervention in MDD patients.

## METHODS

This hospital based longitudinal study was conducted in the Department of Biochemistry, Burdwan Medical College & Hospital, West Bengal, India. Clinically diagnosed 50 drug naive patients of major depressive disorder (MDD) attending psychiatry outdoor of the same institution were selected for this study. All of them were prescribed same selective serotonin reuptake inhibitors (SSRI) class of antidepressive medications. Drug naïve cases were diagnosed as MDD according to the criteria of DSM-IV by consultant psychiatrist, are considered as study population. Lipid profile, salivary alpha amylase and depression were first assessed during first visit of the patients at Psychiatry OPD. Grading of depression was further assessed during follow up after 6 weeks and three months after receiving treatment. Lipid profile and salivary alpha amylase were evaluated after three months.

We included newly diagnosed drug naive patient of MDD aged between 20 and 50 years. Exclusion criteria were: presence of serious medical illness like HIV, Cancer, CKD etc. (assessed through physical examination and routine laboratory screening), any history of drug abuse and presence of another pre or co-existing major psychiatric disorders, e.g., schizophrenia, panic attack, post traumatic stress disorders, etc. Moreover, patients who were unwilling to participate in the study or already having anti-depressant medications or any other drugs that may cause alteration in serum lipid profile were also excluded.

Salivary alpha amylase (sAA) levels were estimated by following Street and Close Method.<sup>10</sup> Reference laboratory range of normal sAA level was set in our Lab by measuring sAA level of 40 healthy subjects (30.8–53.2 IU/ml). The patients were instructed not to have food or drink for 2 hours before the saliva collection. The collection was done in a well ventilated place. The whole saliva samples were collected using a needle less syringe by a slight suction from the floor of the patient's mouth. To control for circadian rhythms, the samples were collected between 9 and 11 am. The saliva collected in first 10 sec was discarded. After this 3 ml of saliva collected. Saliva transferred to an empty pre-sterilized bottle. Centrifugation done for 10–15 mins. Then the supernatant was diluted in normal saline and used for sAA estimation. The optical density of the test and control was measured using semi-autoanalyzer at a filter of 630 nm. Then these values were used for calculations; later the value obtained was multiplied by the dilution factor. Which gave the amylase level in Street and Close units of that particular sample. These values were converted into IU by multiplying with 0.61.

In blood, total cholesterol, triglycerides, HDL-cholesterol all were measured by conventional laboratory methods. VLDL cholesterol was estimated through dividing triglycerides value by 5 (when TG <400 mg/dl) and LDL cholesterol was determined by Friedwald's formula. Depression grading was done by Hamilton depression rating scale (HDR-S) and clinical global impression (CGI-S) scale both of them contained oral questionnaires. All methods were carried out in accordance with relevant guidelines and regulations.

Data was collected, scrutinized, compiled and analysed using SPSS Statistics for Windows, version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normal distribution using Kolmogorov–Smirnov test. Then, the mean values between 0 and 12 weeks were compared by paired Student's t-test between all the lipid parameters, except for sAA for which Wilcoxon Signed Rank test was performed. For the mood status scores using HDR-S and CGI scales, Friedman test was performed, as they were ordinal data and more than 2 observations are there i.e., at 0, 6 and 12 weeks.

Correlation between sAA and lipid profile was done by using Pearson correlation coefficient test

both at 0 and 12 weeks. Similarly, correlations of HDR-S and CGI scales with sAA and lipid profile were done by using Pearson correlation coefficient tests both at 0 and 12 weeks. A p-value <0.05 was considered statistically significant.

## RESULTS

The activity of salivary alpha amylase is elevated at initiation of study and well above the reference value set in our laboratory. After 3 months of anti-depressive therapy with Tab. Sertraline (SSRI) showed significant reduction in sAA activity ( $p<0.001$ ) as shown in Table 1. Among lipid parameters HDL-cholesterol showed a lower value at initiation, gradually became significantly ( $p<0.001$ ) higher after 3 months of therapy. LDL-cholesterol was higher earlier at starting of therapy, showed a significant reduction ( $p<0.01$ ) after 3 months of treatment. The total

cholesterol and triglycerides level did not change significantly before and after therapy ( $p>0.05$ ), as shown in Table 1. At initiation of study, there was no significant correlation found between either of the parameters ( $p>0.05$ ) (as shown in Table 2 & 3); however, there was only significant negative correlation was found between HDL-C level and salivary alpha amylase (sAA) level ( $r=-0.291$ ;  $p<0.05$ ) after 12 weeks of treatment, as shown in Table 2. Two scales were used in this study – Hamilton depression rating (HAMD-R) scale and clinical global impression (CGI) scale on the basis of oral questionnaire and clinical assessment. There was significant reduction in scores in HAMD-R scale and of CGI scale also at 6 weeks ( $p<0.001$ ) and 12 weeks ( $p<0.001$ ) consecutively, clearly showing the improvement in mood status and overall depression as shown in Table 1.

**Table 1:** Comparison of salivary alpha amylase, lipid profile, HAMD-R scale and CGI scale (N=50)

	Salivary alpha amylase	HDL-C	LDL-C	TC	TG	HAMD-R scale	CGI scale
0 week	65.42±9.27	46.54±6.15	136.2±27.84	211.94±26.25	147.55±26.51	19.46±7.35	4.56±1.19
6 weeks	–	–	–	–	–	11.96±5.67	3.6±1.01
12 weeks	57.99±8.39	52.99±7.47	129.77±22.59	214.47±20.63	145.43±23.36	6.5±4.42	2.66±0.82
p-value	<0.001*	<0.001*	<0.01*	>0.05*	>0.05*	<0.001**, <0.001***	<0.001**, <0.001***

\*=comparison between 0 and 12 weeks; \*\*=comparison between 0 and 6 weeks; \*\*\*=comparison between 6 and 12 weeks.

**Table 2:** Correlation between salivary alpha amylase and lipid profile at 0 week and 12 weeks

	HDL-C (0 week)	LDL-C (0 week)	TC (0 week)	TG (0 week)
Alpha amylase (0 week)	$r=0.093$ ; $p=0.521$	$r=0.042$ ; $p=0.77$	$r=0.025$ ; $p=0.861$	$r=0.065$ ; $p=0.653$
	HDL-C (12 weeks)	LDL-C (12 weeks)	TC (12 weeks)	TG (12 weeks)
Alpha amylase (12 weeks)	$r=-0.291$ ; $p=0.040$	$r=-0.191$ ; $p=0.184$	$r=-0.135$ ; $p=0.351$	$r=0.148$ ; $p=0.306$

**Table 3:** Correlation between HAMD-R scale and CGI scale with salivary alpha amylase and lipid profile at 0 week and 12 weeks

	Alpha amylase (0 week)	HDL-C (0 week)	LDL-C (0 week)	TC (0 week)	TG (0 week)
HAMD-R scale (0 week)	r=-0.079; p=0.584	r=-0.826; p=0.860	r=-0.065; p=0.655	r=-0.033; p=0.820	r=0.152; p=0.293
CGI scale (0 week)	r=0.116; p=0.422	r=-0.122; p=0.397	r=0.243; p=0.089	r=0.189; p=0.190	r=-0.200; p=0.165
	Alpha amylase (12 weeks)	HDL-C (12 weeks)	LDL-C (12 weeks)	TC (12 weeks)	TG (12 weeks)
HAMD-R scale (12 weeks)	r=-0.071; p=0.626	r=-0.119; p=0.410	r=0.150; p=0.297	r=0.104; p=0.474	r=0.089; p=0.537
CGI scale (12 weeks)	r=0.023; p=0.875	r=0.052; p=0.719	r=0.004; p=0.981	r=0.015; p=0.918	r=-0.105; p=0.469

## DISCUSSION

A number of biomarkers, such as cortisol and catecholamines, have been found to reliably indicate the reactivity of physiological stress, such as the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullary (SAM) systems. Moreover previous studies that examined the response of sAA to the activity of SAM levels were correlated with increased plasma catecholamine (norepinephrine), indicating sympathetic nervous system activation.<sup>11,12</sup> Measurement of non-invasive parameters like salivary cortisol or sAA in psychosocial stress indicates association of high stress levels with higher sAA levels.<sup>13</sup> In presence of sudden stressful stimuli, sympathetic fibres trigger the salivary gland to secrete amylase before the gland responds to norepinephrine from the adrenal medulla. It is thought faster than the response to norepinephrine, and it usually occurs within minutes. sAA has the potential to become a marker of autonomic activity because salivary gland secretion is regulated by both sympathetic and parasympathetic nerves. Thus, autonomic nervous system in a coordinated way increases salivary secretion.<sup>14</sup>

The activity of salivary alpha amylase is elevated at initiation of study and well above the reference value set in our laboratory. After 3 months of anti-depressive therapy significant reduction was observed in sAA activity ( $p < 0.001$ ). In a previous pilot study, alpha amylase activity and cortisol level in saliva decreased during treatment of suicidal clients of borderline traits, clearly reflects

a significant reduction in values of both salivary cortisol and alpha amylase activity at pre and post session of psychotherapy.<sup>15</sup> Thus, stressful event like MDD in this study has also shown the significant reduction in sAA activity after therapy. Apart from that anti-depression therapy may cause dry mouth as an adverse reaction that may cause the alteration of alpha amylase value in saliva. Evidence showed that dry mouth is the most common among complications during bupropion therapy than conventional SSRI therapy.<sup>16</sup>

Now-a-days, obesity is increasingly linked to impairments in central nervous system (CNS) function. Individuals with obesity have a 55% increased odds of developing depression.<sup>17</sup> There is also a bidirectional association between obesity and depression such that depressed individuals are more likely to be obese due to poor food choices and decreased physical activity.<sup>17</sup> Major depression is associated with reduced formation of cholesteryl esters and perhaps by impairment of reverse cholesterol transport. The later is reportedly accompanied by lower serum HDL-C. Among lipid parameters HDL-C showed a lower value at initiation, gradually became significantly ( $p < 0.001$ ) higher after 3 months of therapy. LDL-C was higher earlier at starting of therapy, showed a significant reduction ( $p < 0.01$ ) after 3 months of treatment. The total cholesterol and triglycerides level did not change significantly before and after therapy ( $p > 0.05$ ). Previous studies showed low HDL-C and high LDL-C among psychiatric patients including MDD in comparison with normal healthy

controls,<sup>18,19</sup> which signify the future possible untoward CVS outcome or insulin resistance as a part of metabolic syndrome. Evidence indicates that disturbances of fatty acids and phospholipids metabolism can play a part in a wide range of psychiatric, neurological and developmental disorders in adults.<sup>20</sup> HDL-C and LDL-C showed increasing and decreasing trend respectively indicating the improvement of the deranged lipid parameters.<sup>20,21</sup>

However, there are a lot of controversies about the impact of several group of anti-depressant drugs on serum lipid profile. In recent studies, conventional SSRI like sertraline or fluoxetine presented a very negligible impact on serum lipid profile.<sup>22,23</sup>

## CONCLUSION

To conclude, major depressive disorder as a part of stress has a close relationship with sympathetic overactivity, HPA axis activation and increased sAA level. MDD as a part of metabolic syndrome

also well associated with dyslipidemia. Thus, salivary alpha amylase and serum lipid profile may act as diagnostic as well as prognostic biochemical indicators for MDD patients.

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**Ethical approval:** This study was approved by the Institutional Ethical Committee of Burdwan Medical College, West Bengal, India.

**Authors' contribution:** S Koley was involved in conceptualization and design of the study as well as patient selection and data collection. S Koley and A Sur were equally involved in data compilation and analysis as well as manuscript preparation, editing and final submission.

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