Effect of Therapeutic Interventions on Salivary Alpha Amylase and Lipid Profile in Major Depressive Disorder Patients

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Research Article

Abstract

Background

Major depression, a disease status as well as a psychosocial burden. High Salivary alpha amylase (sAA) level and dyslipidaemia have been observed in few occasions of Major Depressive Disorder (MDD) patients.

Results

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 = 0.004) level respectively. Single significant negative correlation found between HDL-C level and sAA level (r = − 0.291, p = 0.04) after 3 months of treatment.

Conclusion

sAA and serum lipid profile can be used as biochemical indicators in Major Depressive Disorder patients.

Introduction And Background:

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 remissions and exacerbations (1). Stress response mimics similar episodes and also 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& activation of sympathetic system (2).The stress response of salivary alpha amylase has been suggested as an index for sympathetic nervous system activation (3). 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. (4)

On the other hand, depression may have an association with metabolic syndrome (5). It has been characterized by increased waist circumference, triglyceride, blood pressure, fasting blood glucose, and low HDL cholesterol (6) (7).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 (8).Laboratory findings reveals 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 (9).

Subjects And Methodology:

Subjects:

It was a hospital based longitudinal study .Clinically diagnosed 50 drug naive patients of major depressive disorder (MDD) in the age group of 20–50 years attending psychiatry outdoor were consecutively studied. 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 TR 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.

INCLUSION CRITERIAS:-

- Newly diagnosed drug naive patient of MDD aged between 20–50 years of age group.

EXCLUSION CRITERIAS:-

- Presence of serious medical illness like HIV, Cancer, CKD etc. (assessed through physical examination and routine laboratory screening.)
- Any drug abuse.
- Presence of another pre or co-existing major psychiatric disorders like Schizophrenia, Panic attack, Post traumatic stress disorders etc.

Patients unwilling to participate in the study or had already received anti-depressant medications or were taking any drugs that may cause serum lipid profile alterations were excluded from the study.

All experimental protocols were approved by Institutional Ethical Committee. Detailed informed consent was obtained from all participants.

Methods :

Salivary alpha amylase level was estimated following Street and Close Method (10), lab range of normal sAA level was set at our Lab by measuring sAA level of 40 healthy subjects ((30.8–53.2 IU/ml). The attendants were instructed not to give him/her 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 circirdian rhythms, the samples were collected between 9–11 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 min. 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 Lab methods. VLDL cholesterol calculated by dividing triglycerides value by 5 (when TG < 400 mg/dl) and LDL cholesterol was calculated 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 Analysis :

All the data were analysed using SPSS software version 17. Continuous variables were tested for normal distribution using **Kolmogorov – Smirnov Test**. Insignificant 'p' values of this test indicates normal gaussian distribution except for the sAA which showed the skewness in distribution of data at 12 weeks. Then the Mean values between 0 and 12 weeks were compared by **Paired 't' test** between all the lipid parameters except for sAA for which **Wilcoxon Signed Rank Test** was performed. For the Mood status scores using HDRS & 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.

However, the correlation between the normally distributed parameters i.e. sAA and lipid profiles was done by **Pearson Correlation** test at 0 week. As the values of sAA was not normally distributed, **Spearman rho Correlation** study was done between sAA and Lipid profile at 12 weeks as well as correlation between these parameters with the scores of each of the two scales done by **Spearman rho Correlation** study at both 0 and 12 weeks.

Results And 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 (11)(12). Measurement of noninvasive parameters like salivary cortisol or sAA in psychosocial stress indicates association of high stress levels with higher sAA levels (13). 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 increase salivary secretion. (14)

The activity of salivary alpha amylase is elevated at initiation of study and well above the reference value set in our lab. 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**. 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 (15). 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. But Croft et al, **1999** found dry mouth is most common complications during bupropion therapy than conventional SSRI therapy done in this study.

Presently, obesity is increasingly linked to impairments in central nervous system (CNS) function. Individuals with obesity have a 55% increased odds of developing depression.(16) 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.(17)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($p = 0.004$) after 3 months of treatment. The total cholesterol($p = 0.199$) and triglycerides($p = 0.176$) level didn't change significantly before and after therapy as shown in **Table – 1.**

A previous cross-sectional study showed low HDL-C and high LDL-C among Psychiatric patients including MDD in comparison with normal healthy controls (18) (19) that describes the future possible untoward CVS outcome or insulin resistance as a part of metabolic syndrome. Increasing evidence indicates disturbances of fatty

acids and phospholipids metabolism can play a part in a wide range of psychiatric, neurological and developmental disorders in adults.(20) In this study, HDL-C and LDL-C showed increasing and decreasing trend respectively indicating the improvement of the deranged lipid parameters.

There is lot of controversy about the impact of several group of anti-depressant drugs on serum lipid profile. In a recent study, conventional **SSRI** like Sertraline or Fluoxetine etc. have presented with a very negligible impact on serum lipid profile(21) (22). In this study, Tab. Sertraline **(SSRI)** was given as anti-depressive medications.

At initiation of study, there is no significant correlation found between either of any parameters of this study as shown in **Table-2** and **Table-3** except at follow up there is only single significant negative correlation found as shown in **Table-2(r = − 0.291, p = 0.04)** between salivary alpha amylase and HDL cholesterol which also shown in a scatter plot in**Figure-1**.

Two scales have been used in this study to assess mood status. One is Hamilton Depression Rating scale (HAMD) and another is Clinical Global Impression Scale (CGI) on the basis of oral questionnaire and clinical assessment. There is significant reduction found in scores in HAMD-R scale at 6weeks (p < 0.001) & 12weeks (p < 0.001) and in scores of CGI scale also at 6weeks (p < 0.001)& 12weeks (p < 0.001) consecutively, clearly showing the improvement in mood status and overall depression as shown in **Table − 1**.

Tables & Figures:

Table − 1: Difference (Mean ± SD) between study parameters i.e. Salivary alpha amylase, Lipid profile, Hamilton depression rating scale scores & clinical global impression scale scores at specified duration with their level of significance. (p value)

(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	136.28 ± 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*	0.004*	0.199	0.176	< 0.001#, < 0.001**	< 0.001#, < 0.001**

*: p value at comparison between 0 & 12 weeks ; # : p value at comparison between 0 & 6 weeks ; ** : p value at comparison between 6 & 12 weeks ; -: Test not done.

(SD = Standard Deviation, p = Statistical Significance, N = Sample size.)

Table 2

:Correlation between Salivary alpha amylase and Lipid profile at 0 week & 12 weeks of study.

	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)
(r = Corretional Coefficient, p = Statistical Significance, * = Significant negative correlation)				

Table-3 :Correlation between Hamilton depression rating scale scores & Clinical global impression scale scores with Salivary alpha amylase & lipid profile at 0 week &12 weeks of study.

	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)

(r = Corretional Coefficient, p = Statistical Significance.)

Scatter diagram showing the only significant negative correlation of this study between sAA& HDL-C at 12 weeks.

Conclusion:

In conclusion, Major Depressive Illnesses as a part of Stress have an established close relationship with sympathetic over activity, HPA Axis activation and increased sAA level. MDD as a part of Metabolic syndrome also well associated with Dyslipidaemia. Thus, Salivary Alpha Amylase (sAA) and Serum Lipid Profile may act as diagnostic as well as prognostic biochemical indicators for MDD patients.

Declarations

Ethics approval and consent to participate:

All experimental protocols were approved by Institutional Ethical Committee before starting the study. Detailed informed consent was obtained from all participants.

Consent for publication:

The authors hereby give consent for publication of this research article.

Availability of data and materials:

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

Satyajit Koley wrote the main manuscript. Arindam Sur prepared the figures & the statistics. Both authors reviewed the manuscript.

Conflict of interest:

The authors would like to declare that there was no conflict of interest in the study.
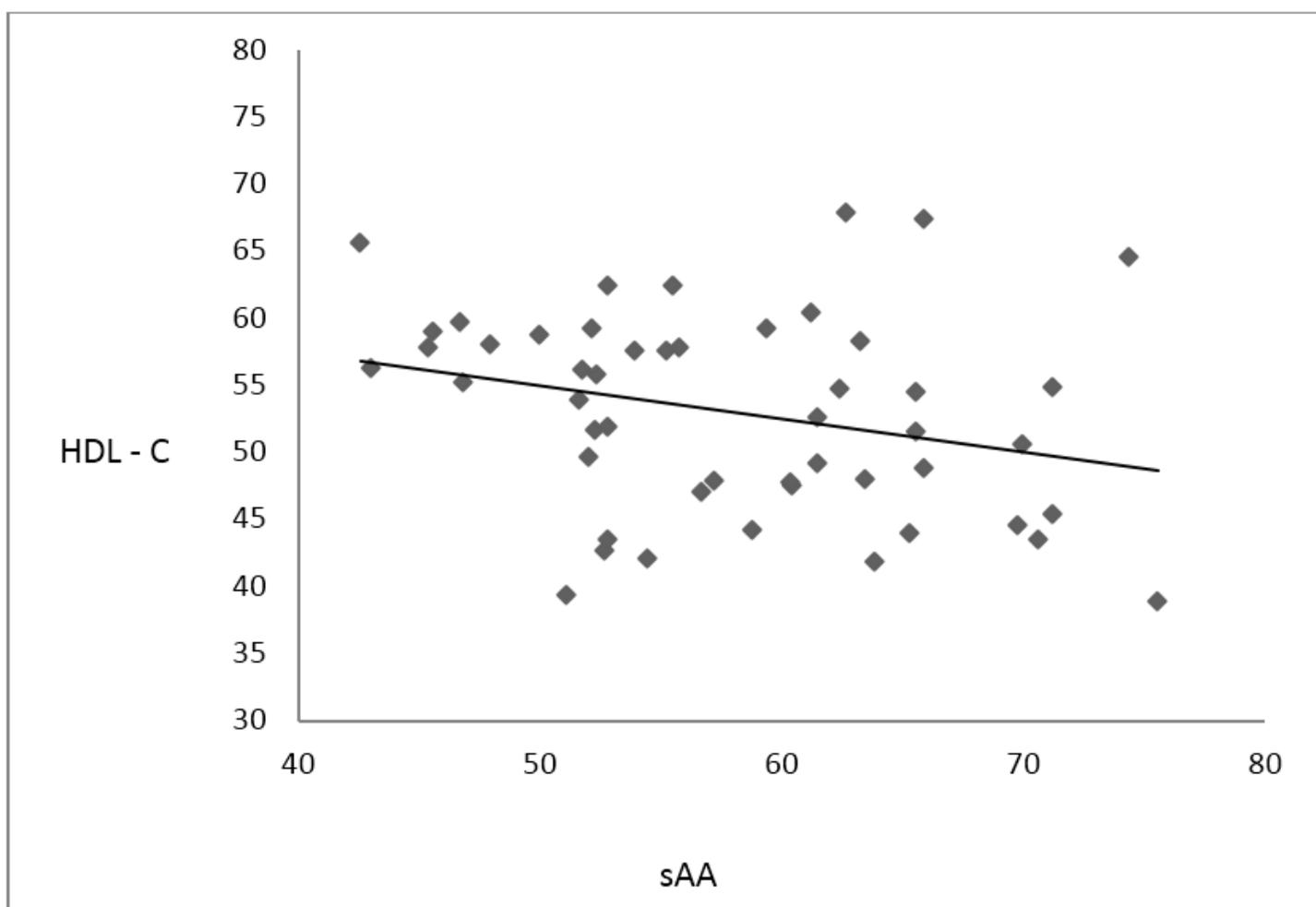
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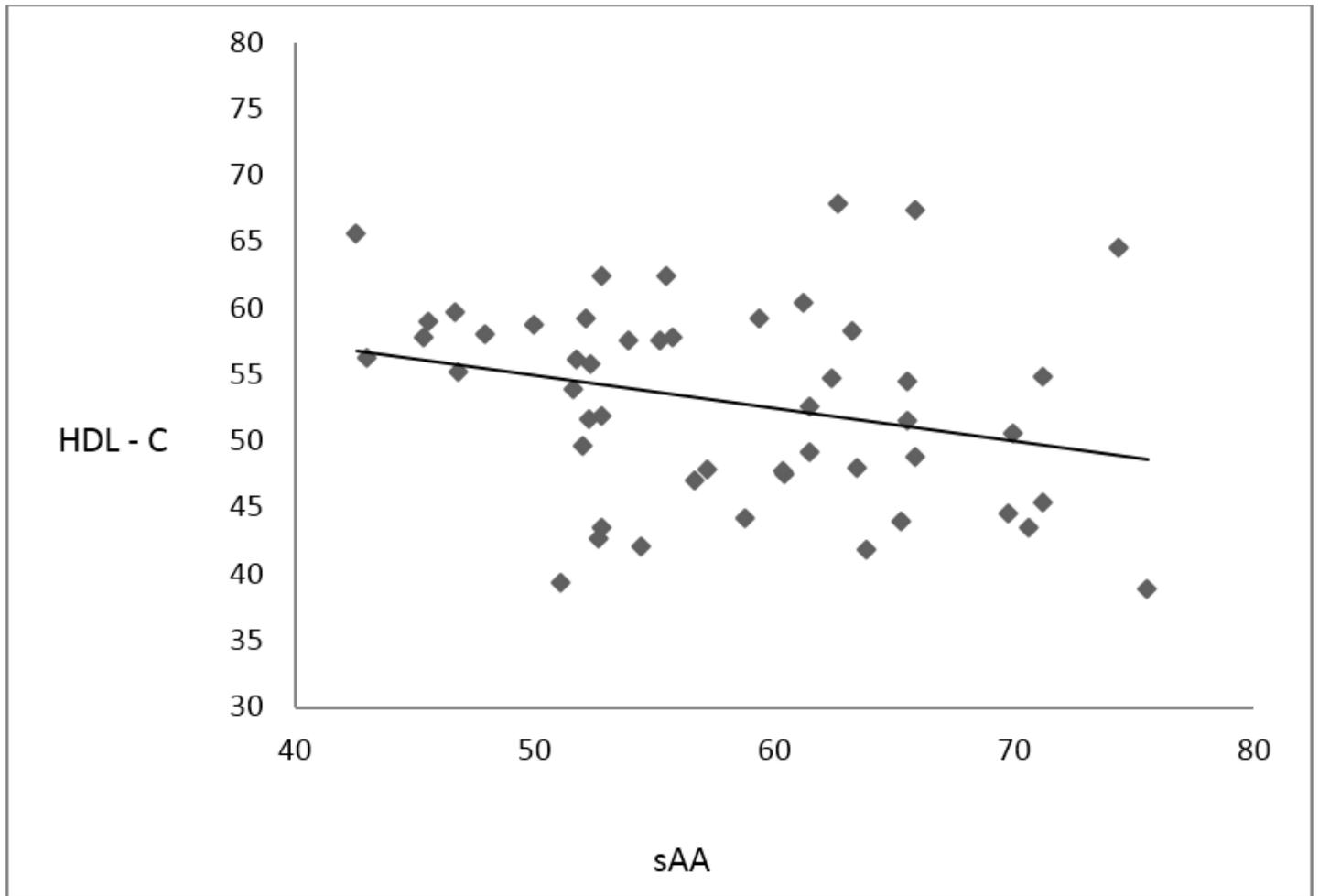
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Figures

Figure 1

Scatter diagram showing the only significant negative correlation of this study between sAA& HDL-C at 12 weeks.
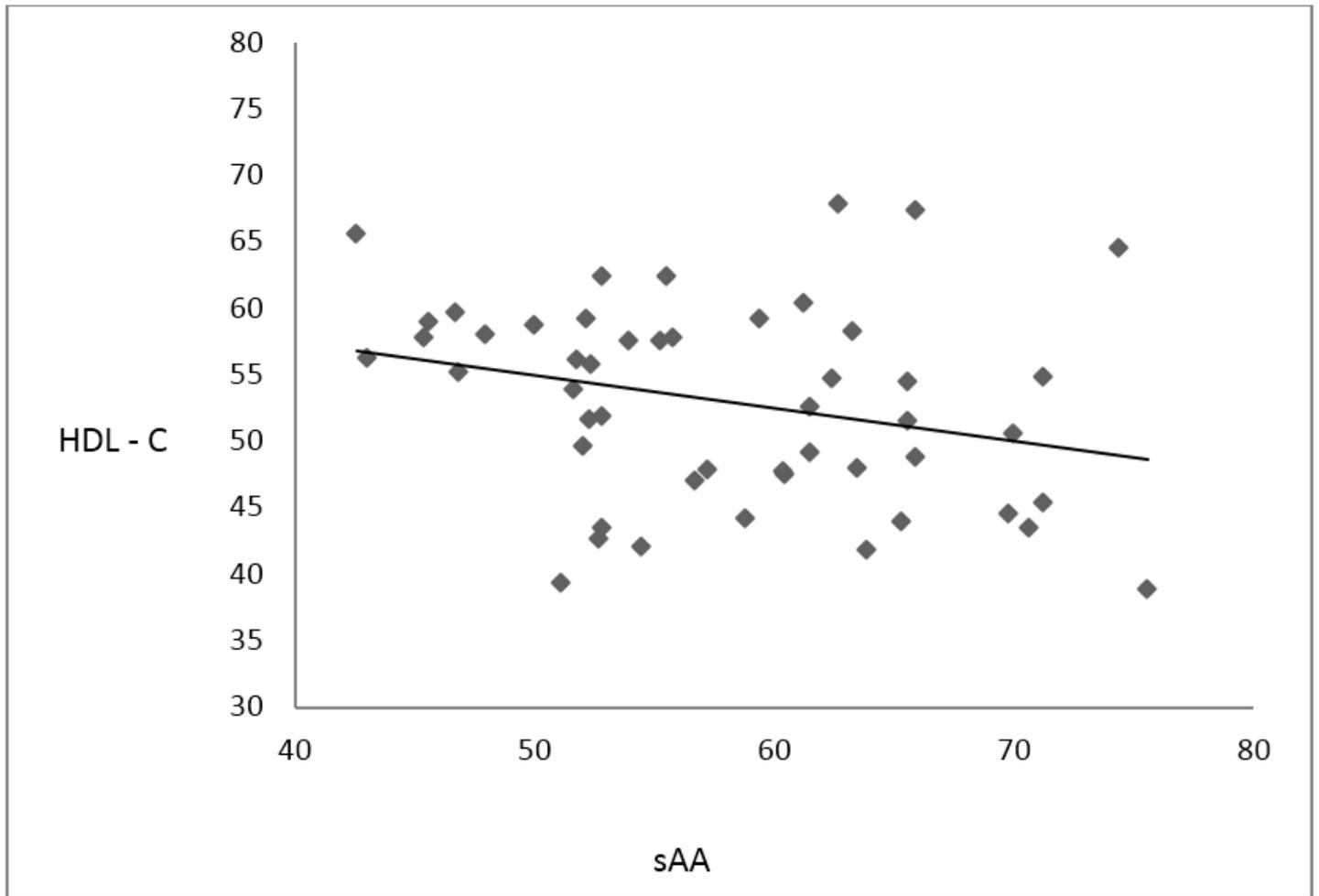
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