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Study of Association and Correlation between Biomarkers and Cardiovascular Risk Factors in Depression: A Cross-Sectional Study

Dr. Himanshu Phulwari, Dr.Paramjeet Singh, *Mukesh Chand Daderwal, Dr. Gunjan Solanki, Dr.Kanwarjeet Singh

Junior Resident, Dept of psychiatry SMS Medical college and hospital, Jaipur, Rajasthan
Senior professor and head of the department of psychiatry
SMS Medical college and Hospital, Jaipur, Rajasthan
MD psychiatry Senior Resident, Dept of Psychiatry,SMS Medical college and Hospital, Jaipur, Rajasthan
Associate professor, dept of psychiatry SMS Medical college and Hospital, Jaipur, Rajasthan

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ABSTRACT:

Introduction: Depression is one of the most common mental illnesses and prevalence is 2.68% in Indian. Depression increases the risk of cardiovascular events. A study was done to quantify the correlation and association between biomarkers and cardiovascular risk factors in depression.

Methodology: Socio-demographic profile of cases and controls was compared using the Chi-square test. For normally distributed quantitative continuous variables were compared using an independent T-test. Pearson Correlation was applied to see the correlation between biomarkers and severity of depression. A Scatter plot was made to graphically represent the correlation. ANOVA test was applied to compare two groups.

Result: There was a significant difference between cases and controls in terms of mean Framingham score (P-value 0.00). The correlation coefficient between Framingham score and biomarkers in cases were 0.33 for NL ratio, 0.18 for TSH, 0.13 for cortisol and -0.25 for vitamin which significantly more than healthy controls.

Conclusion: There was a significant correlation found between the Framingham score and all the biomarkers including TSH, Neutrophil lymphocyte ratio (NLR), cortisol and vitamin D.

Keywords: Depression, Neutrophil lymphocyte ratio, Cortisol, TSH, Vitamin D**,** Framingham score

I. INTRODUCTION

Depression is one of the most common mental illnesses. The prevalence of depression worldwide is 5%(1). The prevalence of depression in India is 2.68%(2). It is also the leading cause of disability worldwide andin India(3).

Patients in depression feel less energy level and adopt a more sedentary lifestyle(4). Patients are at risk of impaired glucose tolerance which may further lead to an increased risk of diabetes and dyslipidaemia. A patient's negative effect makes him/her more prone to a substance like smoking (5). Smoking increases the risk of atherosclerosis. (4). Depression and stress are related to an increase in blood pressure (6–8). All of these mechanisms lead to an increased risk of Cardiovascular disease (CVD) in patients with depression.Many have found a positive correlation i.e. increased cardiovascular risk has been found in patients with depression (9,10).It will be useful to establish this depression and cardiovascular risk correlation further in this study.

Increased levels of tumour necrosis factor (TNF) and other pro-inflammatory cytokines as CRP, fibrinogen, and interleukin-1 and interleukin 6 are often observed in depressed patients as well as in an inpatient with metabolic syndrome and CVD (11–13). So, immune mediators may be a common cause of depression and CVD(14).

Inflammation and oxidative stress have been implicated in the pathophysiology of cardiovascular disease.So inflammatory biomarkers have been in the spotlight (15).N/L ratio is a novel inflammatory marker that is associated with the severity and prognosis of cardiovascular disease(16).Studies show that among patients undergoing Percutaneous Trans coronary angioplasty (PTCA), those who had an increased Neutrophil lymphocyte ratio had a poorer prognosis. So increased cardiovascular risk is associated with an increased neutrophil-lymphocyte ratio(18, 19).

Thyroid and hormones have direct and indirect actions on the regulation of lipid production disposal and efflux. Overt hypothyroidism is associated with dyslipidaemia. Dyslipidaemia is a primary major risk factor for

atherosclerotic disease and overt hypothyroidism and is associated with an increased prevalence of ischemic heart disease (19,20)(21,22).Serum TSH is positively and linearly associated with serum total cholesterol and increases total cholesterol in patients with Coronary Heart Disease (23). So Hypothyroidism can increase cardiovascular risk in the population and therefore, it will be useful in predicting cardiovascular risk severity.

Cardiovascular risk (CVR) and its relation with cortisol have limited studies. Most of these studies have been performed on subjects who had either iatrogenic Cushing syndrome or Cushing's disease and found an increased risk of cardiovascular disorders in these patients (24,25).

Depression is associated with higher cortisol levels, non-suppression of endogenous cortisol after dexamethasone administration, and alteration in circadian rhythms.Diabetes mellitus and hypertension were seen more in hypercortisolism patients (26–28). These changes in the HPA axis determine important cardiovascular alterations that can lead to cardiovascular disease(29).

It will be useful to find out the correlation between CVR and cortisol.

Proposed mechanisms include the effect on the Renin-Angiotensin system (RAS), on glycaemic (30–32).Vitamin D deficiency is a negative regulator of RAS, so it acts as an antihypertensive agent. In a study, when mice were given vitamin D suppression of RAS was seen(33,34).Early studies have suggested that vitamin D-deficient rodents are not able to adequately secrete insulin compared with vitamin D-sufficient controls(35). Several studies, including one published by Scragg et al, demonstrated that lower vitamin D status was associated with an increased risk of diabetes(36,37).

In this study, we will try to find out the correlation between CVR and vitamin D.

II. METHODOLOGY

Across-sectional study was conducted at the Outdoor and Indoor service at Psychiatric Centre,Sawai Man Singh Medical College, Jaipur.Clearance from the ethical committee was taken. The study period was from June 2019 to August 2020.

The objectives of the study wereto see the association between depression and cardiovascular risk and also to see the correlation between cardiovascular risk factors and NL ratio, TSH,cortisol, Vitamin D inpatientas well as inhealthy controls. 120 cases and 120 healthy controls were taken. Inclusion criteria for the patients were diagnosed witha depressive episode as per ICD-10, age 18 years to 59 years, either sex, with informed consent and literate enough to understand and perform a questionnaire. Patient with any inflammatory disease, hematopoietic system disorders, history of (h/o) malignancies/chemotherapy, acute infection and chronic inflammatory status, acute coronary syndrome, h/o using glucocorticoid therapy in the past 3 months, h/o of chronic renal or hepatic disease, h/o Substance other than tobacco and h/o other psychiatric disorder were excluded.

Inclusion criteria for healthy controls wereage 18 to 59 years, either sex, participants to give informed consent, literate enough to understand and perform a questionnaire. Exclusion criteria were the same for the patients.

A screening Performa was applied which contained all the exclusion criteria in yes/no format, socio-demographic details, history of suicide attempt by the patient or the family, number of episodes, duration of the illness, age at onset of the illness, number of hospitalizations, family history of affective disorders. Hamilton Depression Rating Scale (HAM-D) was applied to quantify the severity of depressionthe and Framingham cardiovascular risk factor Prediction tool(Sydell and Arnold Miller 1998) was used to assess cardiovascular risk factors.

Laboratory investigations were done which included Neutrophil/lymphocyte ratio, Serum TSH,Serum cortisol and Serum vitamin D.

Qualitative variables included gender, marital status, educational level, socio-economic statuswere statistically compared between cases and controls using the Chi-square test. For normally distributed quantitative continuous variables like age, the two groups were compared using an independent T-test.Pearson Correlation was applied to see the correlation between biomarkers and severity of depression. A Scatter plot was made to graphically represent the correlation. ANOVA test was applied to compare two groups. A 95% confidence interval was taken and $p < 0.05$ was considered to be statistically significant.

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III. RESULTS:

Table1:Showing mean and standard deviation(SD) of Framingham score in bothcasesand controls

Category	Framingham score
Cases Mean [SD]	13.4[5.4]
Control Mean [SD]	10.7[4.6]
Test statistic [p value]	**4.02 [0.00]**

Graph 1: showing the correlation between HAM-D score and Framingham score

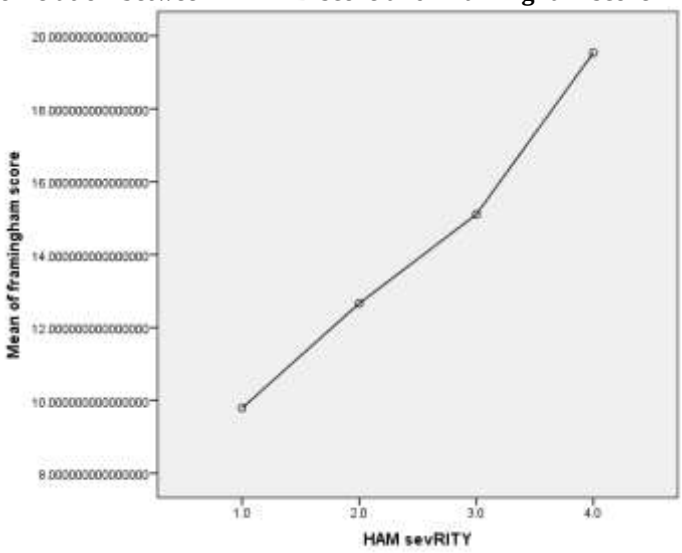

Table2: Correlation of Framingham score with biomarkers among cases

	N/L ratio	TSH	Cortisol	Vitamin D
Mean value [SD]	2.04 [0.6]	5.2[2.1]	27.9[5]	16 [6.6]
Correlation coefficient WithFramingham score	0.33	0.18	0.13	-0.25
P value	**0.00**	**0.04**	**0.02**	**0.00**

Framingham score in cases mean was 13.4 with SD 5.4

Table3:Correlation of Framingham score with biomarkers among control

	N/L ratio	TSH	Cortisol	Vit D
Mean value [SD]	1.6 [0.26]	5.2 [2.1]	-0.06 [0.46]	37.5[7.9]
Correlation coefficient With Framingham score	0.07	0.07	-0.06	0.24
P value	0.44	0.12	0.49	0.009

Framingham score in controls 10.7 with SD 4

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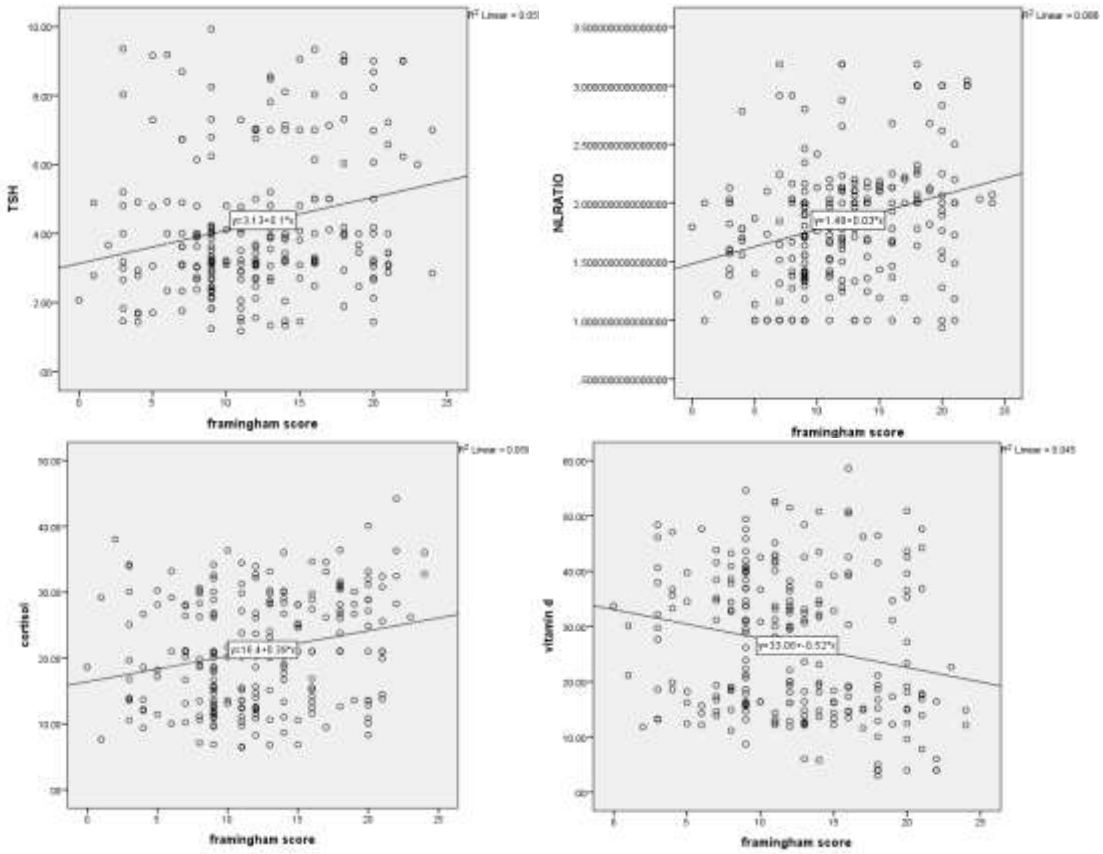
Tables2 and 3 showing the correlation between the Framingham score and its correlation with biomarkers among cases and controls. Among cases, the Framingham score had a positive correlation with N/L ratio, TSH, and Cortisol while the inverse correlation with vitamin D. Correlation was statistically significant with N/L ratio and TSH and vitamin D.



Graph 2: Above graphs shows the correlation between Framingham score and cortisol, vitamin D, NL ration and TSH

IV. DISCUSSION

In this study mean Framingham score in cases was 13.4 with a standard deviation (SD) of 5.4 and in controls as 10.7 with SD 4.6. Framingham score was higher in cases compared to controls. It was statistically significant (p=0.00) (9). Probably cases had a higher cholesterol level due to a sedentary lifestyle (38). In this study, also there was a significant correlation between the severity of depression and cardiovascular risk factors. As the severity of depression increases, cardiovascular risk also increases(39).

In this study, the correlation between Framingham Score and N/L ratio was statistically significantcompared to controls(39).

In this study, it was found that the correlation between Framingham score and TSH was statistically significant compared to controls(40)(41)(42).

There is an inverse correlation between Framingham and vitamin D. People with vitamin D deficiency are more prone to develop cardiovascular disease(30)(43).

In this study, a positive correlation between Framingham and cortisol which was statistically significant compared to controls was found. This study is the first to see the correlation between Framingham and cortisol. Hypercortisolaemia causes more diabetes and hypertension risk leads to increase cardiovascular risk(26–28)(44).

V. CONCLUSION

This is a cross-sectional study to see the association of cardiovascular risk and depression in patients of depression and healthy controls. This study found that cardiovascular risk is more in patients with depression than healthy controls.This

study also found that as the severity of depression increases cardiovascular risk also increases. Cardiovascular risk had a positive correlation with NLR,TSH and cortisol and an inverse correlation with serum vitamin D.

VI. LIMITATIONS AND FUTURE DIRECTIONS

This was a cross-sectional study which might not allow a definitive conclusion about the causal link between cardiovascular risk and depression and also cardiovascular risk and biomarkers. The sample size was small.The duration of illness and number of episodes were not considered. Further studies require for definitive conclusions.

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