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BIOCHEMICAL ANALYSIS IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER IN JAMMU POPULATION

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ABSTRACT: The study was conducted to study biochemical parameters in 42 major depressive disorder (MDD) patients, 22 males and 20 females (age range 18 - 55 years) visiting the Psychiatric Department, Government Medical College, Jammu. The smoking and alcohol intake was much lower (95.24% and 88.09%) in patients (both male and female) diagnosed with MDD. The well being status is also 76.19% satisfactory with 71.43% patients with no family history of psychiatry illness and 73.81% with absence of chronic morbidity. The levels of thyroid stimulating hormone (TSH), ferritin and insulin are in normal reference range while the Vitamin B and Vitamin D 25OH levels are observed to be lower in 54.76% patients. The present study concluded that there is need for awareness towards these biomarkers as they play an important role in brain functioning by planning awareness programs. Therefore, further study with large sample size to evaluate these biochemical parameters and other risk factors is required to mitigate the effect of depression in the population of Jammu.

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 work¹. Epidemiologist, national and international agencies have been sounding an alarm on rapidly rising burden of depression for past many years. According to WHO², in young people neuropsychiatric disorders are the leading causes of worldwide disability and second leading cause of death in 15 - 29 year.

Kessler *et al.*,³ found that approximately 16% of adults would experience depression in their lifetime. It is a major public health problem affecting in large number to human clan of any age: children, adolescents, middle- aged groups and the elderly; residing either in urban or rural areas and linked with premature death by suicide and other causes⁴, disability and economic burden⁵.

There are several factors responsible for depression, *viz.* biological, social, economic and cultural factors, out of all strongly associated factors with mental disorders are social deprivation and poverty⁶⁻⁸. The rise of depression prevalence in recent years is due to demographic shifts to urban areas, rapid social and economic changes, sedentary lifestyles and earlier pubescence. According to Charles *et al.*,⁹ in India, there has been seen significant changes *viz.* globalization,

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urbanization, migration, and modernization coupled with rapid socio- demographic transition, which may likely to increase depression in the coming years. In India, one in 20 *i.e.* 5.25% people with age group over 18 years have suffered from depression at least once in their lifetime¹⁰.

There are different mechanisms involved in developing depression. For many diseases and disorders, depression itself is both the cause and consequence and is also associated with today's modern life style that may contribute to metabolic abnormalities. There are different risk factors involved- biochemical, genetics, personality and environmental factors. Nutritional deficiency in any form can lead to impairment of our nervous system, which may lead to depression to the people at any age². For development and functioning of brain, Vitamin D (a unique neurosteroid hormone)¹¹; iron^{12, 13}; thyroid stimulating hormone¹⁴ are important as they are involved in many neurological processes including neuroimmuno-modulation, regulation of neurotrophic factors, neuroprotection, neuroplasticity and brain development^{15 - 17}, therefore, plays an important role in depression.

There were many cross-sectional^{18 - 20}, interventional^{21 - 22} studies conducted on association of Vitamin D with depression and have shown significant association in many studies^{23 - 24}. The association of some other Vitamin deficiencies *viz.* folic acid, Vitamin B12, niacin and Vitamin C with depression has also been observed¹⁶. Thyroid and insulin also play an important role in manifestation of mental health, as with increase or decrease of these parameters can cause mood changes and disturbance at emotion level.

There are number of studies^{25 - 30} carried out on Indian population which reported prevalence of depression in different geographical regions of India while till date no study has been conducted on scenario of depression in the Jammu city of J&K state. Therefore, keeping in mind the increasing prevalence of depression globally, the present study was conducted on the population of Udhampur, Jammu city with the following objectives:

- To analyze different biochemical parameters (Vitamin D25OH, Vitamin B12), iron

(ferritin), thyroid stimulating hormone and insulin in MDD patients.

- To study the association of biochemical parameters with depression in MDD patients.

MATERIALS AND METHODS:

Study Design and Data Collection: The study was conducted after getting the approval from Institutional Ethical Committee on outpatients visiting the Psychiatric Department, Government Medical College, Jammu, from August 2016 to January 2017. During this duration, a total of 60 patients with current major depressive disorder were selected and 42 patients fulfill the criteria for the present study. The inclusion and exclusion criteria for the present study is as follows:

Inclusion Criteria: Patients aged between 18 to 55 years, diagnosed for mental disorders in accordance with Diagnostic and Statistical Manual³¹ (DSM-V) with the use of neuropsychiatric interview.

Exclusion Criteria: The patients on any type of medication or with any other disorder were excluded from the present study. Patients suffering from lifetime history of mania or hypermania or any with concurrent psychotic symptoms or pregnant females were also not included.

After informed written consent, their socio-demographic information was recorded on the pre-designed questionnaire and the rate of severity of depression in MDD patients was measured using the Hamilton Rating Scale of Depression³² (HRSD, 1960). The British Columbia Cognitive Complaints Inventory (BC-CCI)³³ is used to measure perceived cognitive problems in depression and Hindi Cognitive Screening Test³⁴ was calculated. For biochemical analyses, 5ml of intravenous blood sample was collected in centrifuge tubes.

Biochemical Analyses: Serum 25-OH Vitamin D, Insulin, Vitamin B12, Thyroid – stimulating hormone (TSH) and Ferritin levels were determined by ARCHITECT assay (Abbott Laboratories, Abbott Park, Illinois, US) an immunoassay using Chemiluminiscent Micro-particle Immunoassay (CMIA) technology, referred to as Chemiflex. The lab references are 20-60 ng/ml for 25-OH Vitamin D; 1 - 300 μ U/mL for

Insulin; 187 - 883 pg/ml for Vitamin B12 0.2700 - 4.2000 μ IU/mL for TSH and 4.63 - 204.00 ng/mL for Ferritin.

Statistical Analysis: The statistical analysis was done using SPSS 15.0 version. The categorical variables in numbers were analyzed using the Chi-squared test for deviations (if any) between male and female participants. The continuous variables of demographic and biochemical parameters were presented as mean \pm S.E.M. (standard error of mean). Pearson correlation analysis was carried out to find the association (if any) of the confounding (independent) variables with biochemical parameters (dependent variables). The significance was considered with *p* values less than 0.05.

RESULTS: A total of 42 MDD patients were studied with gender distribution of 22 males (52.38%) and 20 females (47.62%), age ranging from 18-55 years with majority (85.71%) of the participants belonging to Hindu community.

Descriptive data of the study population is presented in **Table 1**. Average ages of major depressive disorder male and female subjects were 40.68 ± 2.63 and 40.85 ± 2.18 years, respectively. The smoking and alcohol intake was much lower (95.24% and 88.09%) in patients (both male and female) diagnosed with MDD. The well being status of MDD patients in the present study is also 76.19% satisfactory with 71.43% patients with no family history of psychiatry illness and 73.81% with absence of chronic morbidity.

The chi-squared analysis revealed no statistical significant difference within male and female patient for religion, place of residence, educational status, family status (living in join or nuclear family), well being status, family history of depression or any psychiatric disorder, HRSD (depression) scale **Table 1**. Therefore, for further analysis the data was pooled. **Table 2** represents the continuous variables of the present study as mean \pm SEM.

TABLE 1: DESCRIPTIVE VARIABLES OF THE MAJOR DEPRESSIVE DISORDER PATIENTS

Demographic	Category	Male (n=22)	Female (n=20)	χ^2 (p value)	Total (%)	
Religion	Hindu	19	17	0.015	36 (90)	
	Muslim	03	03		06 (10)	
Place of Residence	Rural	14	11	0.324 (0.569)	25 (59.52)	
	Urban	08	09		17 (40.48)	
Marital Status	Unmarried	04	00	-	04 (9.52)	
	Married	18	16		34 (80.95)	
	Widow	00	04		04 (9.52)	
Employment	Employed	Professional	03	02	-	05 (11.90)
		Skilled	10	02		12 (28.57)
		Unskilled	04	00		04 (9.52)
	Unemployed	-	01	16	17 (40.48)	
Family status	Nuclear	09	10	0.349 (0.554)	19 (45.24)	
	Joint	13	10		23 (54.76)	
Education	Literate	05	09	2.338 (0.126)	14 (33.33)	
	Illiterate	17	11		28 (66.67)	
Socioeconomic Status	Lower	10	09	-	19 (45.24)	
	Middle	12	10		32 (76.19)	
	Upper	00	01		01 (2.38)	
Smoking	No	20	20	-	20 (47.62)	
	Yes	02	00		02 (4.76)	
Alcohol	No	17	20	-	37 (88.09)	
	Yes	05	00		05 (11.90)	
Chronic Morbidity	Present	03	06	1.667 (0.196)	09 (21.43)	
	Absent	19	14		33 (78.57)	
Disease	Present	05	06	0.286 (0.592)	11 (26.19)	
	Absent	17	14		31 (73.81)	
Wellbeing	Poor	07	03	1.633 (0.201)	10 (23.81)	
	Satisfactory	15	17		22 (52.38)	
Family History	Absent	17	13	0.773 (0.379)	30 (71.43)	
	Present	05	07		12 (28.57)	

Grades of Depression	Mild	01	05	3.973	06 (14.29)
	Moderate	12	07	(0.264)	19 (45.24)
	Severe	07	06		13 (30.95)
	Very Severe	02	02		04 (9.52)
Cognitive behaviour	BC-CCI-E ^a	00	01	-	01 (2.38)
	Moderate	09	08		17 (40.48)
	Not at all	02	02		04 (9.52)
	Quite a bit	11	09		20 (47.62)
	Some	21	18	0.469	39 (92.86)
	HSCT ^b	01	02	(0.493)	03 (7.14)
Thyroid Stimulating Hormone (µIU/ml)	<0.27	00	01	-	01 (2.38)
	0.27-4.2	22	18		40 (95.24)
	>4.2	00	01		01 (2.38)
Ferritin (ng/ml)	<4.63	01	00	-	01 (2.38)
	4.63-204	21	20		41 (97.62)
	>204	00	00		00
Vitamin B 12 (pg/ml)	<187	12	11	-	23 (54.76)
	187-883	08	09		17 (40.48)
	>883	02	00		02 (4.76)
Vitamin D 25OH (ng/ml)	<20	12	11	-	23 (54.76)
	20-60	07	04		11 (26.19)
	>60	03	05		08 (19.05)
Insulin (µIU/ml)	1-300	22	20	-	42 (100)

Chi-square test reveals no significant difference within male and female patients

^aBC-CCI-E: British Columbia Cognitive Complaint Inventory; ^bHCST- Hindi Cognitive Screening Test

TABLE 2: CONTINUOUS VARIABLES OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Biochemical Parameters	Total (n = 42)
Thyroid Stimulating Hormone (µIU/ml)	1.80 ± 0.16
Ferritin (ng/ml)	36.45 ± 5.13
Vitamin B12 (pg/ml)	296.57 ± 49.33
Vitamin D 25OH (ng/ml)	32.71 ± 4.46
Insulin (µIU/ml)	14.78 ± 1.18

Biochemical Parameter Analysis: The levels of thyroid stimulating hormone (TSH), ferritin and insulin are in normal range according to the reference ranges in major depressive disorder patients while the Vitamin B and Vitamin D 25OH levels are observed to be lower in 54.76% patients

Table 1. Table 3 represents the levels of different biochemical parameters in accordance with grade of depression and observed that the level of TSH is significantly higher in individuals with moderate depression.

TABLE 3: COMPARISON OF BIOCHEMICAL PARAMETERS USING STUDENTS t-TEST IN ACCORDANCE WITH GRADES OF DEPRESSION

Grades of Depression	Number of Patients	Thyroid Stimulating Hormone (µIU/ml)	Ferritin (ng/ml)	Vitamin B12 (pg/ml)	Vitamin D 25OH (ng/ml)	Insulin (µIU/ml)
Mild	06	2.46 ± 0.55	26.20 ± 5.46	241.33 ± 90.04	26.50 ± 8.59	15.28 ± 2.46
HR Moderate	19	2.02 ± 0.21 ^{*a}	38.28 ± 7.91	240.00 ± 36.93	36.68 ± 7.79	15.32 ± 1.98
SD Severe	13	1.28 ± 0.27 ^a	39.18 ± 11.01	439 ± 140.13	27.34 ± 6.72	15.32 ± 2.24
Very severe	04	1.44 ± 0.37	34.28 ± 16.47	185.25 ± 45.34	40.66 ± 16.11	9.73 ± 0.21

^{*a}(p < 0.05)

Stress Level and Severity of Depression: There was no significant correlation of biochemical parameters observed with well-being of patient and severity of the depression observed (Table not shown).

25OH in MDD patients, that is similar to the observation by Schneider and co-workers³⁵, which reported lower Vitamin D levels in persons with schizophrenia and major depression when compared to healthy controls.

DISCUSSION: The present study revealed decreased levels of Vitamin B12 and Vitamin D

Wilkins *et al.*,³⁶ also claimed association of Vitamin D deficiency with the presence of an

active mood disorder as assessed by the depressive symptoms inventory. The mechanism explaining association of Vitamin D with mental disorders is not clearly understood, but there are studies reporting their association with brain development. Eyles *et al.*,³⁷ reported that there are Vitamin D receptors in the hypothalamus, which may be important in neuroendocrine functioning. Some studies have reported that Vitamin D is important for brain development³⁸⁻³⁹. The level of Vitamin D is lower in dark-skinned individuals, due to higher melanin levels. Therefore, they experience reduced subcutaneous Vitamin D synthesis in comparison to those with lighter pigmentation, making them another high-risk group for Vitamin D deficiency⁴⁰.

Our results for TSH levels does not go with other studies showing significant increase of TSH levels in patients with unipolar depression^{41, 42}, with major depressive disorder⁴³. The comparison within depressed subjects with and without psychotic features showed significantly higher levels of TSH in subjects with psychotic symptoms⁴⁴. The levels of insulin and ferritin were within the normal range. Hunt and Pete⁴⁵ showed no significant association with depression while some studies reported significant iron deficiency in infants⁴⁶; mothers⁴⁷. Iron plays an important role in brain⁴⁸, as it is required for dopamine synthesis, an important neurotransmitter in mood disorders⁴⁹.

CONCLUSION: The cause and consequence of depression is several non-communicable diseases (NCDs) such as cancer, ischemic heart disease and diabetes, substances use disorders (alcohol and drugs) and nutritional disorders (under-nutrition, over-nutrition and obesity) and depressed people are more likely (1.5 times) to die than general population⁵⁰ due to untreated problem, which is expected to increase over twenty years⁵¹.

Therefore, there is a need for the awareness to the population about these common biomarkers along with signs of sadness, loss of interest or pleasure, feeling of guilt or low esteem, disturbed sleep or appetite, tiredness and poor concentration, which affect our brain functioning and should be evaluated at early stage of illness. However, this study needed to be further established with multicenter and larger-scale study.

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