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Salivary Cortisol Levels in Severely Depressed Patients and Healthy Individuals

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ABSTRACT

Introduction: *This study compared the levels of salivary cortisol in patients suffering from severe depression and in healthy individuals.* ***Methods:*** *Sample size included 30 diagnosed cases of major depression based on outdoor clinical assessment (from April 2015 to December 2105) and was established by ICD-10 and DSM-IV criteria and 30 physically and mentally healthy subjects. In this study diagnosed cases of hyperaldosteronism, Cushing's syndrome/ disease were omitted. A predesigned proforma was created on the basis of Becks Inventory. Saliva samples were collected and processed, and the measurement of cortisol levels was done by ELISA.* ***Results:*** *In a normal subject, the mean cortisol level was 1.46 ± 0.9 µg/dl (Mean ± SD) whereas in depressive patients it was raised (2.2 ± 1.6 µg/dl, p=0.031). Results also showed that high level of cortisol in saliva was found in individuals with a positive family history of depression (2.3 ± 1.8 µg/dl) as compared to healthy subjects (1.5 ± 1.0 µg/dl). Mean BMI was also found to be different between the 2 groups (p=0.012).* ***Conclusion:*** *We concluded that salivary cortisol may act as an early diagnostic tool and non-invasive biomarker for prompt diagnosis of potential cases of depression for effective management. Hence, early initiation of treatment can be helpful in improving the late clinical consequences in severely depressed patients and decreasing the morbidity.*

Keywords: Depression, Saliva, Cortisol, Family history, Biomarker

INTRODUCTION

Depression is a common mental global disorder affecting all races, cultures and geographical locations characterized by sadness, loss of interest in daily life activities, feeling of guilt and tiredness, disturbed sleep or appetite and poor concentration [1]. World widely, 350-355 million people are affected by depression including both the genders of any age [2,3]. Approximately 16% of populations might have suffered an episode of depression one-time in their lives [4].

Globally, the WHO has anticipated that depression will be the principal cause of debility by 2020 [5]. Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5) states, depression is characterized by sadness, feeling of loneliness or ill-tempered mood [6]. Among the 3 types of depression (mild, moderate and major), a person having Major Depressive Episode (MDE) presents with complaints of mood disturbance and the person feels disheartened, dejected and useless [7]. In MDE, these symptoms are prolonged and persist for more than 2-weeks. The person is confined to himself and does not like to interact with anybody. Hopelessness and worthlessness increase to the extent that the person may even start thinking of suicidal ideas [8]. Loss of loved ones, unemployment, divorce, morbid diseases, amputations or radical surgeries may trigger depression. The pathophysiology of depression involves a chemical imbalance in the neurotransmitters, like serotonin, noradrenaline, and cortisol along with structural changes including neuronal atrophy and denaturation occurring in the brain [9].

Depression has been found to be associated with increased cortisol levels. Cortisol, a glucocorticoid is measurable in plasma, saliva and urine samples. Cortisol assays may be useful to observe the effects of acute and chronic stress [10].

Cortisol and depression have a deep and incredible connection [11]. Raised cortisol levels result in an increase in salivary secretions. Therefore, salivary cortisol can be used as an early diagnostic biomarker for this ailment [12]. Moreover, no exceptional training or equipment is essential to gather salivary samples [13].

The objective of the study was to compare salivary levels of cortisol in patients with severe depression and normal healthy individuals and to determine salivary cortisol as a probable biomarker for severe depression.

MATERIALS AND METHODS

This cross-sectional analytical study was carried out in the Physiology Department, Shaikh Zayed Federal Postgraduate Medical Institue Lahore and Punjab Institute of Mental Health Lahore, Pakistan. Total of 60 participants aged between 18-60 years was included in this study, they were divided equally into 2 groups as normal healthy individuals with no physical or mental illness and severely depressed groups. On outdoor clinical assessment the patients were categorized as patients of severe depression, then were further confirmed by ICD-10 and DSM-IV criteria. Personal data including name, gender, age, BMI and education status along with the general physical health, family history of depression were recorded in predesigned proforma. Detailed medical history and physical examination of each subject were performed. Patients were considered as a case of severe depression on the basis of clinical assessment and were confirmed by Beck's inventory [14,15]. The subjects suffering from Cushing's syndrome/disease, hyperaldosteronism and pregnancy were excluded. Early morning saliva samples were collected (subjects were asked not to eat, drink or brush teeth before sample collection). Before collecting the samples all the subjects were asked to rinse the mouth with normal saline, and saliva samples (4-5 ml) were taken in clean glass tubes and were stored at -20ºC for 24 hours. The samples were centrifuged at 20,000 rpm for 10 minutes, transferred to Eppendorf, properly labeled and stored at -20ºC for 30 days till further analysis. Salivary cortisol levels were estimated by ELISA. SPSS version 20.0 was used and the collected data was entered and analyzed, $p \leq 0.05$ was considered statistically significant.

RESULTS

Out of total 60 subjects, there were 14 (46.67%) males and 16 (53.33%) females in each normal and depressive group respectively with mean age 35.7 ± 6.8 years (normal group) and 39.1 ± 11.6 years (depressive group, p=0.177). Normal subjects had mean BMI 22.02 ± 4.21 kg/m^2, whereas depressive patients had 24.64 ± 3.58 kg/m^2, showing a significant difference in mean BMI between both the groups (p=0.012) (Table 1).

Table 1 Comparison of height, weight, and BMI in both study groups

Variables		Mean (µg/dl)	S.D	Minimum	Maximum	p-value
Height	Normal	1.67	0.08	1.52	1.85	0.056
	Depressive	1.63	0.08	1.55	1.83	
Weight	Normal	61.55	11.61	42.90	99.80	0.151
	Depressive	65.79	10.92	40.80	86.70	
BMI	Normal	22.02	4.21	16.20	35.20	0.012*
	Depressive	24.64	3.58	16.80	31.90	
p-value ≤ 0.05						

Regarding the association of depression with family history, 17 (56.67%) depressive patients had a positive family history of depression as compared to normal healthy individuals (10.00%) who did not show a family history of depression (Figure 1).

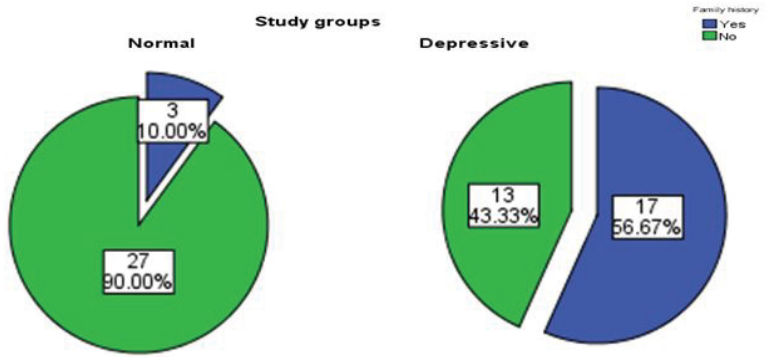

Figure 1 Comparison of family history in both study groups; **p-value<0.001 (significant association of family history and depression)

Moreover, the depression score was also found to be significantly high in depressed subjects along with raised salivary cortisol levels (Table 2)

Table 2 Depression score in normal and depressed subjects

Variables	Study Groups	Mean	S.D	Minimum	Maximum	Median (IQR)[a]	p-value
Depression	Normal	5.73	4.05	1	16	5 (5.50)	<0.0001
score	Depressive	52.03	5.08	41	62	52 (7.25)	

Mean cortisol levels were found significantly higher (p=0.031) in depressive patients (2.23 ± 1.69 µg/dl) as compared to normal subjects (1.46 ± 0.91 µg/dl) (Table 3).

Table 3 Comparison of cortisol levels in both study groups

Variables	Study Groups	Mean (µg/dl)	S.D	Minimum	Maximum	p-value
Cortisol	Normal	1.46	0.91	0.36	4.33	0.031*
	Depressive	2.23	1.69	0.35	6.34	

DISCUSSION

Depression is a curable mental disorder if it is diagnosed earlier and managed adequately. Cortisol levels in saliva were observed to be elevated in patients suffering from major depression as matched to healthy individuals and people having a positive family history of depression were more prone to develop depression.

Cortisol and depression have a deep-rooted relationship with each other. These results are in consistent with a study carried out by Herbert, et al., [11]. They found a higher level of cortisol in saliva in major depression illness individuals [7]. A remarkable relationship between salivary cortisol and depression was also observed by Yonekura, et al., [16]. Similarly, Hanson, et al., studied raised cortisol levels during stress [17]. Likewise, Goodyer, et al., predicted high morning cortisol levels might be a cause of depression [18].

The results can be elaborated by the fact that the adrenal glands release cortisol under the effect of the Hypothalamic-Pituitary-Adrenal axis (HPA axis). Hence, the main reason for raised salivary cortisol levels in depression is owing to the hyperstimulation of this HPA axis.

In this study, we also found that high BMI and depression were positively associated (p=0.017). These results are in consistent with a study who also found that if higher the BMI the greater the chances of development of depression [19]. Moreover, a statistically significant association between depression and its family history was also observed. Similar results were also found by Monroe, et al., [20,21].

On the contrary, there are few studies that suggested that raised salivary cortisol is not related to depression rather the salivary levels are decreased [22,23].

The lowered level of salivary cortisol in these studies could be explained by the overexertion or exhaustion of hypothalamic-pituitary-adrenal axis leading to its depression.

CONCLUSION

This study compared the salivary cortisol levels in severely depressed patients and normal individuals and found significantly raised salivary cortisol levels in severely depressed patients as compared to normal individuals. Salivary cortisol might be considered as a prognostic and diagnostic marker in depression for future research initiatives. Similarly, high BMI also had a significant relationship with salivary cortisol levels.

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DECLARATIONS

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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