Serum Cortisol in Patients with Major Depressive Disorder and Those with Substance Abuse Disorder in Benin City. A Pilot Study

Adewolu Olanike[1] F, OwieG[2] O

[1] Department Chemical pathology, University of Benin Teaching Hospital
[2] Federal Psychiatric Hospital, Benin City

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Corresponding author email:

nikemide2@yahoo.com

Abstract

Major depressive disorder (MDD) is a psychiatric illness with growing psychosocial concern, intensified by socio-economic and political stressors. Depression is associated with hyperactivity of the hypothalamo Pituitary Adrenal(HPA) axis. Meanwhile, dysregulation of HPA axis has also been reported in substance abuse disorder.

Aim

To evaluate serum cortisol levels among patients with major depressive disorder, patients with substance abuse disorder, and healthy controls, in order to determine the presence of HPA axis dysregulation.

Materials and method

This was a prospective cross sectional pilot study carried out in 2 mental health facilities in Benin city in July 2024. 33 subjects participated in the study. 13 diagnosed with MDD, 10 diagnosed with substance abuse disorder and 10 healthy controls. Serum cortisol was assayed using Quantitative immunoflourescence method. Fasting plasma glucose was assayed by glucose oxidase method. Statistical Analysis used SPSS 26 with t-tests and Pearson's correlation; Level of significance at $p \leq 0.05$.

Results

Mean serum cortisol was significantly higher in MDD subjects (345.91±195.45 nmol/L) compared with controls (203.38±63.46) p=0.03. Similarly, mean serum cortisol was higher in Substance abuse subjects (268.47±150.23nmol/l) compared with controls (203.52±63.46 nmol/l); however the difference was not statistically significant (p=0.38). In addition, mean fasting plasma glucose was higher in MDD (105.30±30.96) then in controls (92.80±17.88) although not statistically significant (p=0.59). In substance abuse subjects, fasting plasma glucose was also higher(98.33±18.72) then in controls (92.80±17.88) but also not statistically significant (p=0.79).

Conclusion

The significantly elevated serum cortisol observed in subjects with MDD, and the higher but non-significant cortisol levels in subjects with substance abuse disorder, suggest possible HPA axis dysregulation. Although fasting plasma glucose levels were higher in both patient groups, the differences were not statistically significant, indicating a trend that may be related to stress-associated hormonal changes and requires further investigation in larger studies.

Key Words: Serum Cortisol, Major depressive disorder (MDD), Substance abuse disorder, Hypothalamo

Introduction

Major depressive disorder (MDD) is a common and debilitating psychiatric condition and a leading cause of disability worldwide, affecting more than 264 million people[1,2]. It is associated with significant psychosocial impairment, reduced quality of life, and increased risk of suicide[3]. In recent years, socio-economic instability and chronic psychosocial stressors have contributed to the rising burden of depressive disorders, particularly in low- and middle-income countries. One of the most consistently implicated biological systems in the pathophysiology of MDD is the hypothalamo–pituitary–adrenal (HPA) axis. Depression is associated with hyperactivity of the Hypothalamo pituitary Adrenal axis (HPA)[1]. Cortisol serves as a biological marker of stress and anxiety[1]. Amongst the most biological phenomena involved in chronic stress throughout life and consequently in MDD is the change in the HPA axis function[4,5,6]. Several studies[4,7] have demonstrated significantly higher serum or plasma cortisol levels in patients with MDD compared with healthy controls, supporting the role of chronic stress and neuroendocrine dysfunction in depression.

Altered functioning of the HPA corticol axis may hold clues to the nature of the motivational changes accompanying addiction and vulnerability to addiction[8]. The economic recession, insecurity and sociopolitical crisis in the world today has plunged some into substance abuse and drug dependency syndrome. The HPA Axis may be a useful system for studying psycho-physiological reactivity in persons who may vary in cognitive, emotional and behavioral tendencies associated with addiction and risk for addiction[8].

Few studies have directly compared serum cortisol levels in patients with MDD and those with substance abuse disorder within the same population. This pilot study therefore evaluates serum cortisol and fasting plasma glucose levels in patients with major depressive disorder and substance abuse disorder in Benin City, Nigeria, with the aim of identifying possible HPA axis dysregulation and associated metabolic trends.

Materials and method

This was a prospective cross sectional study, involving a total of 33 subjects. 13 diagnosed with Major depressive disorder (MDD), 10 with substance abuse disorder and 10 healthy subjects as controls. They were recruited consecutively from two psychiatric health facilities in July 2024, after meeting the inclusion criteria. Informed consent was obtained for the study. Relevant medical history and data was obtained using a structured questionnaire.

Inclusion criteria for both Major depressive disorder and substance abuse disorder.

- Newly diagnosed patients
- No associated comorbidity

Exclusion criteria

- Patients with chronic depressive disorder or chronic substance abuse disorder
- Patients with associated comorbidity

Sample collection

6mls of fasting venous blood was collected at 8am under aseptic conditions and dispensed into plain bottles (for serum cortisol assay) and fluoride oxalate sample bottle (for plasma glucose). Samples were centrifuged and dispensed in plain bottles and stored at 20℃ until analysis.

Biochemical Analysis

Serum cortisol was assayed using the fluorescence immunoassay technology, which involves the use of a sandwich immune detection method. When sample is added to the sample well of test cassette, the fluorescence-labelled antibody binds to the cortisol in blood specimen. As the sample mixture migrates on the nitro cellulose matrix of test strip, the cortisol-antibody complex is captured to a fixed antibody in the test strip. The more cortisol in the blood specimen, the more complexes accumulated in the test strip. Signal intensity of fluorescence of detector antibody reflects amount of cortisol captured and shows cortisol concentration in the blood specimen.

Plasma glucose was assayed using the glucose oxidase method where glucose is oxidized to gluconic acid and hydrogen peroxide which alongside peroxidase reacts with phenol and 4-aminoantipyrine to form quinoneimine. The absorbance of the colored complex, proportional to the concentration of glucose in the specimen is measured at 500 nm.

Statistical Analysis

This was done using IBM SPSS version 26. Difference between means of variables was established using the student "t" test. Person's correlation was used to determine correlation between the variables. Level of significance was established at $p \leq 0.05$.

Results

A total of 33 subjects were recruited for the study, 13 diagnosed with depressive disorder (MDD), 10 with substance abuse disorder and 10 healthy age and gender match subjects as controls.

Mean age of subjects with MDD, Substance abuse disorder was 34.91±10.09 years, 25.11±5.40 years respectively (Table1).

Mean Systolic and diastolic blood pressure in MDD subjects, Substance abuse disorder subjects was (110.91±10.44 mmHg, 67.27±7.8 mmHg), (103.33±5.77 mmHg, 70.00±10.00mmHg) (Table 1).

Table 1: Demographics of subjects with MDD and Substance Abuse

	Major Depressive Disorder n=13	Substance Abuse n=10
Male	8 (61.5)	8(80%)
Female	5 (38.5)	2(60%)
Age (years)	34.91±10.09	25.11±5.40
Systolic Blood Pressure (mmHg)	110.91±10.44	103.33±5.77
Diastolic Blood Pressure (mmHg)	67.27±7.8	70.00±10.00

Serum Cortisol Levels in MDD and Substance Abuse Disorder

Mean Serum cortisol in MDD subjects was higher (345.91±195.45nmol/L), than that of the controls (203.52±63.46 nmol/l). The difference was statistically significant (P=0.03) (Table 2) (Figure 1). Mean Serum cortisol was higher in subjects with Substance abuse disorder (268.47±150.23nmol/l) compared with the controls (203.52±63.46 nmol/l). However, in this case, the difference was not statistically significant (P=0.38).(Table 2) (Figure 1).

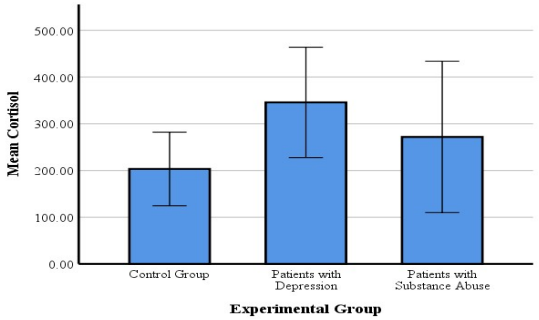

Figure 1: *Mean serum cortisol levels in patients with major depressive disorder, substance abuse disorder, and healthy controls.*

Fasting Plasma Glucose Levels in Study Groups

Mean fasting plasma Glucose in MDD subjects was higher (105.38±30.96 mg/dl), compared with that of the controls (92.80±17.88 mg/dl), but the difference was not statistically

significant p=0.59 (Table 2), Mean fasting plasma glucose was also slightly higher in subjects with substance abuse (98.33±18.7 mg/dl) compared with controls 92.80±17.88 mg/dl. Also, the difference was not statistically significant p=0.79 (Table 2).

Table 2: Serum cortisol, Plasma glucose in Subjects with Major depressive disorder (MDD) and Substance abuse disorder

Parameters	MDD (n=13)	Substance Abuse (n=10)
Cortisol (mmol/l):	Subject 45.91±195.45	268.47±150.23
	Control 203.52±63.46	203.52±63.46
	P value0.03*	0.38
Glucose (mg/dl)	Subject 05.30±30.96	98.33±18.72
	Control 92.80±17.88	92.8±17.88
	P value 0.59	0.79

*statistically significant

Serum cortisol showed a weak negative correlation with duration of disease diagnosis and stay in hospital in subjects with MDD, r= -0.152, which was not statistically significant P=0.67 (Table 3), Serum cortisol also showed a weak positive correlation with Systolic and diastolic blood pressure r=0.087, r=0.171, respectively which was not statistically significant p=0.78, p=0.57 respectively (Table 3).

Table 3: Correlation of Serum cortisol with Systolic blood pressure, diastolic pressure and duration of disease diagnosis and stay in hospital

Parameter	r	p value
Systolic Blood pressure	0.087	0.59
Diastolic Blood pressure	0.171	0.78
Duration of disease diagnosis and stay in hospital	-0.152	0.67

Discussion

The socio-economic crisis over the world has made incidence of cases of depression and substance abuse to be on the increase. This is a worldwide phenomena, understanding of the precipitating factors, the pathophysiology in these disease conditions will go a long way in proper treatment, management of patients and positive outcomes. The mean age of subjects with both depression and substance abuse, was below 40years. This is a pointer to the fact that the younger generation which is the most productive part of the society, are being affected by these mental health challenges. Mean Serum Cortisol level was significantly higher in MDD subjects compared with the controls. Several studies [1,4,7,9] have reported higher levels of serum or plasma cortisol in patients with MDD. The higher levels of serum cortisol in these subjects is suggestive of disturbances or dysregulation in the hypothalamo pituitary adrenal axis in these group of patients. One of the subjects in the study had hypercortisolism, therefore monitoring of serum or plasma cortisol in patients with depression may be of use both in early detection of subjects who develop dysregulation of hypothalamo pituitary adrenal axis or even Hypercortisolism, or it may even play a role in monitoring of response to therapy.

Mean serum cortisol level was higher in subjects with Substance abuse disorder, though not statistically significant. Lovallo[8] reported that chronic heavy intake of alcohol and nicotine may cause modification in frontal- libic interactions and may account for HPA response differences seen in alcoholics and smokers. Yibrah[10] et al in their own study among males with substance abuse reported that there was significant difference in cortisol level between subject and controls. This observations shows that further studies still need to be done on HPA function in substance abuse disorder.

It was observed that mean fasting plasma Glucose was slightly higher in MDD subjects compared with controls, with some of the

subject having values falling into impaired Glucose tolerance category. This indicates a need for further investigation. Knol[11] et al, reported in their study that depressed adults have a 37% increased risk of developing type 2 diabetes mellitus. The observation in the current study along with that of Knol[11] et al maybe suggestive that monitoring plasma glucose in patients with MDD may be useful for early detection of glucose intolerance. Shuangyu[12] et al reported 9.28% of hyperglycaemia among patients with MDD hospitalizes for the first time. Difference between fasting plasma glucose in subject with substance abuse was just slightly higher than in controls. Ojo[13] et al reported that people who abuse substance are at increased risk of metabolic syndrome and diabates resulting partly from increase cell damage and due effect of opoids on glucose homeostasis. Serum cortisol also showed a weak negative correlation with duration of disease diagnosis and stay in hospital in subject with MDD. Though this was not statistically significant, it may however suggest, that once patients are diagnosed and therapy commenced, whether pharmacotherapy and psycotherapy, the dysregulation or abnormality in the hypothalamic adrenal axis may be corrected and serum or plasma cortisol levels begin to fall. While Burgess[14] etal reported a reduction in serum cortisol levels after electroconvulsive therapy, Nandem[15] et al, however did not find a convincing relationship between cortisol levels and therapeutic response in either a clinical or preclinical study. Alenko[16] et al also reported no significant difference in cortisol levels before and after treatment in patients with depressive disorders.

A study by Ligabue[17] et al reported that treatment retention was associated with cortisol levels and those with above normal cortisol levels presented a worse prognosis related to treatment retention. Also Huntington[18] in his study reported that participants who remained in the treatment program less than 90 days had significantly higher cortisol levels. These observations maybe suggestive that cortisol levels may play a role in predicting prognosis in these patients.

Conclusion

The significantly elevated serum cortisol observed in subjects with MDD, and the higher but non-significant cortisol levels in subjects with substance abuse disorder, suggest possible HPA dysregulation. Although fasting plasma glucose levels were higher in both patient groups, the differences were not statistically significant, indicating a trend that may be related to stress-associated hormonal changes and requires further investigation in larger studies.

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