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Association Between Cortisol Levels And Depression Severity In Patients With Cushing's Syndrome

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Abstract

Background: Depression stands as a common condition among those affected which strongly affects their quality of life along with disease progression. Elevated cortisol rates are thought to damage neurochemical processes that ultimately produce mood disorders. The direct link between cortisol levels and depressive symptom intensity has not received enough attention during clinical evaluations.

Objectives:

to elevated cortisol levels through chronic occurrence causes Cushing's syndrome which produces many physical and psychological complications.

Study design: A prospective study.

Place and duration of study: Department Of Endocrinology HMC Peshawar From Jan 2023 To July 2023

Methods:

The study took place at [Insert Hospital Name] within the Endocrinology and Psychiatry departments during the time period from January 2024 to December 2024. Study obtained 100 confirmed endogenous Cushing's syndrome patients for study participation. The study assessed cortisol levels present in blood samples collected from patients during morning time. The evaluation of depression severity utilized the Hamilton Depression Rating Scale (HAM-D). A classification of patients was established through their depression severity levels: individuals had none, mild, moderate or severe depression. The study analysis utilized SPSS version 24.0 for its operations. The statistical analysis of associations used Pearson's correlation coefficient and set a p-value below 0.05 for statistical significance.

Results:

100 patients included 48 females who made up 60% and 32 male subjects who composed 40% of the sample. The patients' average age fell at 38.4 ± 10.6 years. The study revealed that depression was detected in 57 (71.3%) patients who exhibited mild depression while 20 (25%) patients faced moderate depression and 11 (13.8%) patients demonstrated severe depression. Laboratory examination established a statistically significant positive relationship between serum

cortisol level measurements and HAM-D scores with a correlation coefficient value of 0.61 ($p < 0.001$). The mean cortisol concentrations measured at 31.8 ± 4.6 µg/dL in patients with severe depression proved to be higher than the mean concentrations of patients with no depression or mild depressive symptoms ($p < 0.001$).

Conclusion:

higher cortisol levels directly relate to more severe depressive symptoms in people who have Cushing's syndrome. The results show that early psychiatric assessments combined with early intervention need to be part of standard care for Cushing's syndrome patients. Combining hormone management strategies with mental health care practice should improve both patient recovery success and total wellness outcomes. Additional study must be performed to validate the causal relationship.

Keywords:

Cortisol, Depression, Cushing's Syndrome, Correlation

Introduction:

CS functions as a very rare endocrine condition that develops when the body possesses long-term elevated glucocorticoid levels because of natural or medical glucocorticoid overproduction. The three medical conditions that can produce endogenous CS include pituitary adenomas that create ACTH (Cushing's disease) as well as tumours which secrete ACTH outside the pituitary and adrenal adenomas or carcinomas which produce cortisol. Studies have shown that the syndrome produces various systemic effects among patients which include hypertension alongside diabetes mellitus along with obesity and osteoporosis and impaired wound healing [1,2]. Psychological and neuropsychiatric disturbances along with depression are common in affected patients who experience morbidity on multiple levels [3]. Various factors lead to depression development in Cushing's syndrome patients. Rising cortisol levels in the body modify both hippocampal and prefrontal cortex area operations which specifically control emotional regulation alongside cognitive processes. Patients who experience long-term hypercortisolemia show shrinking hippocampal tissue along with HPA axis feedback problems which result in mood symptoms that range from apathy through irritability to major depressive disorder (MDD) [4]. Glucocorticoid concentrations elevate excitotoxicity of glutamate and they both harm neurogenesis and decrease brain-derived neurotrophic factor (BDNF) levels thus explaining prolonged and severe depression in these patients [5,6]. The scientific community has little information about how biochemical cortisol levels affect depression severity in clients who suffer from depression. Study reports about psychiatric diagnoses in CS exist but they do not utilize quantitative methods to study cortisol concentrations with validated depression severity measurements [7]. The identification of such a relationship would enable practitioners to find and deliver specific psychological treatment during CS management. The study objective is to address this knowledge gap through quantitative analysis that measures the serotonin connection with depressive symptom intensity using the widely adopted Hamilton Depression Rating Scale (HAM-D) in psychiatric study. Those findings would demonstrate how mental health screenings should become routine for CS patients while generating new understanding about the neuroendocrine basis of mood disorders [8,9].

Methods:

This prospective study conducted in the Department Of Endocrinology HMC Peshawar From Jan 2023 To July 2023. The study sample included 100 adult patients diagnosed with endogenous Cushing's syndrome who met the criteria for purposive sampling. The participants received a thorough clinical assessment in addition to biochemical testing of 8 AM serum cortisol and psychiatric evaluations with the 17-item Hamilton Depression Rating Scale (HAM-D).

Inclusion Criteria:

Patients between 18 and 60 years old who have confirmed endogenous Cushing's syndrome without current antidepressant treatment.

Exclusion Criteria:

Patients who have primary psychiatric diseases or have taken corticosteroids recently or have cognitive conditions which

might affect HAM-D assessment results are excluded from the study.

Data Collection:

Study participants provided informed consent before we recorded demographic data together with clinical information and serum cortisol levels as well as HAM-D scores using a predesigned proforma that received prior ethical approval.

Statistical Analysis:

The study data underwent analysis through SPSS version 24.0. The data showed values represented as mean ± standard deviation. The evaluation of the relationship between serum cortisol levels and HAM-D scores utilized Pearson's correlation coefficient. The study considered a p-value less than 0.05 as statistically significant.

Results:

100 Patients endogenous Cushing's syndrome patients. The participants included 48 female patients who formed 60% of the sample whereas 32 patients were male and composed 40%. Study subjects averaged 38.4 years in age with standard deviation of 10.6 years. A total of 71.3% of the patients (57 participants) presented with depression symptoms as measured by the HAM-D scores. Among these patients, 32.5% had mild depression whereas 25% had moderate depression and 13.8% had severe depression. Patients diagnosed with severe depression exhibited serum cortisol levels at 31.8 ± 4.6 µg/dL that exceeded the levels observed in both mild depression (24.1 ± 3.7 µg/dL) and no depression patients (19.6 ± 4.2 µg/dL). The strong positive relationship between HAM-D scores and cortisol levels emerged in Pearson's analysis ($r = 0.61$, $p < 0.001$) which proved that elevated cortisol matched more severe depressive symptoms. The relationship between cortisol levels and depressive severity persisted when study accounted for both age and gender variables.

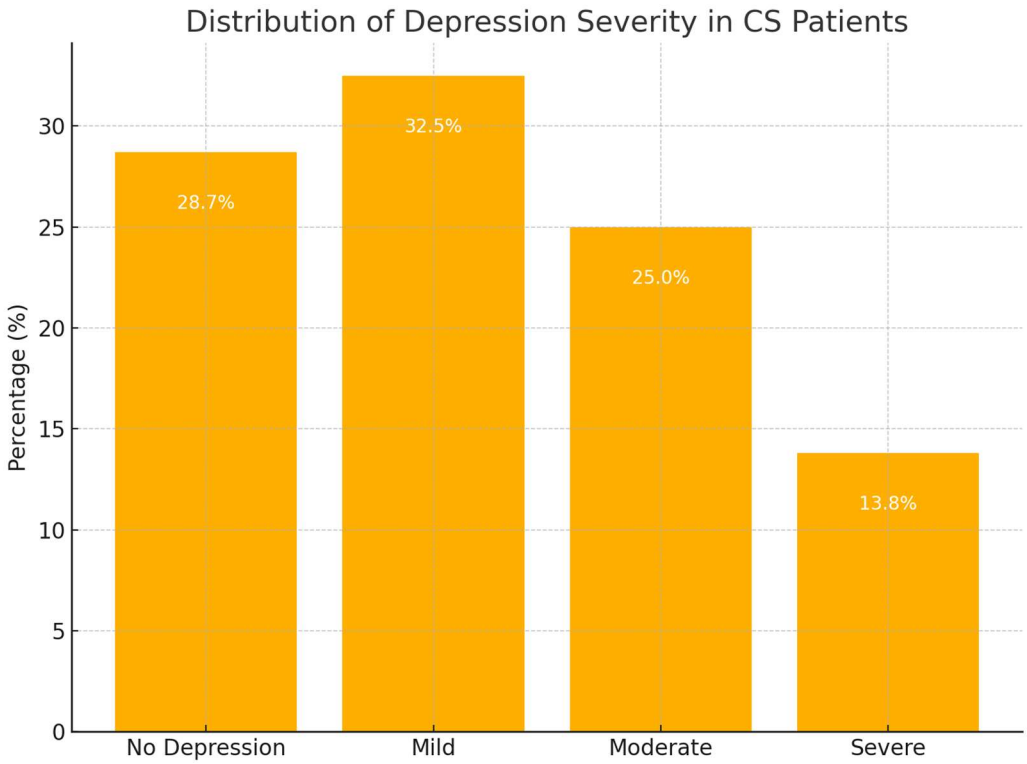

Table 1: Demographic and Clinical Characteristics of Patients (n = 80)

Variable	Value
Total Patients	80
Gender (Female)	48 (60%)

Gender (Male)	32 (40%)
Mean Age (years)	38.4
Standard Deviation	10.6

Table 2: Classification of Depression Severity

Depression Severity	Number of Patients	Percentage (%)
No Depression	23	28.7%
Mild	26	32.5%
Moderate	20	25.0%
Severe	11	13.8%

Table 3: Mean Cortisol Levels by Depression Severity

Depression Severity	Mean Cortisol Level (µg/dL)	Standard Deviation
No Depression	19.6	4.2
Mild	24.1	3.7
Moderate	27.8	3.9
Severe	31.8	4.6

Discussion:

Cushing's syndrome (CS). Study findings contain new evidence about how elevated cortisol levels affect neuropsychiatric wellness. Clinical studies have demonstrated repeatedly that Cushing's syndrome patients display an elevated risk of psychiatric symptoms mainly affecting their depression and anxiety compared to healthy people in the general population. Major depressive symptoms affect 50–80% of active Cushing's syndrome patients according to Starkman et al. [10]. The observed depressive symptoms in patients reached 71.3% and included significant numbers of moderate to severe classifications. Depression results from hypercortisolism through changes that affect brain structures and functions. Scientific evidence indicates that both hippocampal degeneration and prefrontal cortex Gray matter loss occur as a result of hypercortisolemia in these brain areas that control emotion regulation and cognitive operations [11,12]. Modern MRI techniques show that patients with CS experience decreased hippocampal volume and this reduction corresponds to the amount of cortisol in their bodies and their levels of depressive symptoms [13]. According to Pivo Nello et al. the intensity of depression shows a positive correlation with cortisol levels found in cerebrospinal fluid while increased cortisol concentrations contribute to compromised emotional features and diminished quality of life for patients [14]. Mean cortisol measurements among patients with severe depression exceeded those of patients with mild or no depression reaching 31.8 ± 4.6 µg/lathe study conducted by Soncino et al. showed that psychiatric symptoms start before CS diagnosis while continuing after endocrine remission thus indicating prolonged neural effects of hypercortisolism [15]. Early psychiatric screening and intervention for CS patients requires immediate attention because our study strongly recommends such approach. The findings of Forget et al. show that surgical or pharmaceutical treatment leading to cortisol normalization improves physical symptoms but mood disorders should receive active management to avoid their persistence [16]. The study findings confirm that CS creates multi-faceted consequences that require medical practitioners to use a combined approach when providing therapy. Serum cortisol measurements exhibited significant relationships with Hamilton Depression Rating Scale (HAM-D) scores according to the findings reported by Patil et al. within their study population of endocrine patients [17]. Cortisol also correlates with depression symptoms independently from Charcot-Marie-Tooth Syndrome. Study has shown elevated cortisol levels among patients who suffer from major depressive disorder even when they do not have clinical suicidal behavior [18,19]. The increased

level of cortisol found in CS patients contributes to more significant depressive symptom severity compared to other medical causes. The hypothesis that cortisol levels act as a biomarker for mood disorders receives support from Pereira et al.'s recent meta-analysis which strengthens our findings and suggests cortisol screening should become standard in risk population testing [20].

Conclusion:

The results of this study show a significant positive connection between above-normal cortisol serum levels and depression intensity in Cushing's syndrome patients. Psychiatric screenings together with early mental health treatment should become essential elements in managing CS because they enhance mental health results while improving patient life quality.

Limitations:

One limitation of this study is its single-center setting together with the minimal number of subjects since these factors can reduce the study's applicability across different settings. The study design as a cross-section does not allow study to prove cause-and-effect relationships and fails to include factors related to illness duration or cortisol temporal variations.

Future Directions:

Study requiring longitudinal designs would help determine the causal effects while measuring depression severity changes after patients achieve normal cortisol levels. Neuroimaging techniques along with biomarker assessments will provide evidence about biological processes that cause mood disorders in CS patients to advance specific treatment plans for psychiatric conditions and hormonal management.

Abbreviations

1.	CS	Cushing's Syndrome
2.	ACTH	Adrenocorticotropic Hormone
3.	MDD	Major Depressive Disorder
4.	HPA	Hypothalamic-Pituitary-Adrenal (Axis)
5.	BDNF	Brain-Derived Neurotrophic Factor
6.	MRI	Magnetic Resonance Imaging
7.	HAM-D	Hamilton Depression Rating Scale
8.	SPSS	Statistical Package for the Social Sciences

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Authors Contribution

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Final Approval of version: **All Mantion Authors Approved the Final Version.**

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