

# Depression in Focus: Understanding the Contrast between MDD and Cushing Syndrome Related Depression

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## Abstract

Depression is a complex and multifactorial medical condition that poses significant challenges for physicians and psychiatrists. Depression occurs due to various etiological factors, including genetic, environmental, and psychosocial influences. This article delves into the intricacies of depression as a medical dilemma between physicians and psychiatrists as we explore the difference between Cushing Syndrome-related depression and Multiple Depressive Disorder (MDD). Understanding disparities is crucial for the accurate diagnosis and prompt management of these distinct depressive conditions.

**Kew Words:** suicide; attempted; vitamin d deficiency; iran

## Main Body:

Cushing's syndrome-related depression and Major Depressive Disorder (MDD) are distinct clinical conditions despite their shared manifestations of depressive symptoms [1]. Cushing's syndrome, an endocrine disorder characterized by excessive cortisol level, that leads to depression is one of its clinical presentations [2]. The main causes of Cushing syndrome include pituitary corticotrophin adenoma, cortisol-producing adrenal adenomas, adrenal carcinoma and adrenal hyperplasia [3].

Symptoms of Cushing syndrome include hypertension, hyperglycaemia, obesity, osteoporosis, and neuropsychiatric problems like depression, anxiety, and irritability. The pathogenesis of these neuropsychiatric problems occurs due to dysregulation of cortisol secretion, either due to hyperfunctioning adrenal glands or exogenous corticosteroid administration (4). Whereas Major Depressive Disorder (MDD) is a psychiatric condition, that has an enduring state of sadness, anhedonia, and diverse emotional and somatic features. It does not arise from a primary organic aetiology like Cushing's syndrome but is multifactorial, with genetic, environmental, and psychological factors affecting its pathophysiology. MDD is characterised by a group of symptoms like Persistent Depressed Mood Sleep Disturbances like Insomnia, and hypersomnia, Significant Weight Changes like Unintentional weight loss or weight gain, Feelings of worthlessness or guilt, decreased concentration, emotional disturbances leading to recurrent thoughts of death or suicide (5). Hormonal imbalance with excessive cortisol levels seen in Cushing's syndrome contributes significantly to the onset of depression. Cortisol being a vital glucocorticoid hormone involved in mood modulation, regulation and stress response, exerts its effects on the central nervous system. However, MDD does not involve the specific hormonal imbalance as seen in Cushing's syndrome. Instead, it primarily revolves around disturbances in neurotransmitter systems such as Serotonin (5HT<sub>2</sub>),

Norepinephrine, and Dopamine. Altered availability or receptor sensitivity of these neurotransmitters within neural circuits affects mood regulation forming the neurochemical basis of MDD [6]. Diagnosis of depression related to Cushing's syndrome includes evaluating the presence of depressive symptoms alongside clinical evidence of cortisol levels in the body. Screening test includes an increase in free cortisol on 24 hours urine analysis, an increase in late-night salivary cortisol level and no suppression with an overnight low dose of dexamethasone test. [7] Whereas, MDD is diagnosed according to explicit criteria delineated in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). As per DSM-5 criteria: Five or more of the following symptoms have been present during the same 2-week period [8].

1. Depressed mood during most of the day
2. Markedly diminished interest or pleasure in almost all activities
3. Significant weight loss or weight gain (>5% of body weight)
4. Insomnia or hypersomnia almost every day
5. Psychomotor agitation or retardation almost every day
6. Fatigability almost every day
7. Feeling of worthlessness or guilt almost every day.
8. Diminished ability to think or concentrate almost every day.
9. Recurrent thoughts of death, and suicide.

Out of this at least one of the symptoms is either depressed mood or loss of interest or pleasure in activities. The diagnostic process involves specific

depressive symptoms over a minimum duration of two weeks, significant functional impairment, and ruling out alternative organic or psychiatric aetiologies. For management of depression in Cushing's syndrome it includes targeting the underlying causative factors. This involves finding the cause of excessive cortisol production or adjusting exogenous corticosteroid therapy (9). Conventional treatment modalities employed for depression, including psychotherapy and pharmacotherapy with antidepressant agents, may also be implemented. Treatment for MDD typically involves a multimodal approach that includes psychotherapy, predominantly cognitive-behavioural therapy (CBT) (10), and pharmacotherapy with antidepressants. Antidepressant drugs include various classes like Tricyclic acid (TCA) {e.g.: Amitriptyline, Nortriptyline, Imipramine, Clomipramine}, Selective serotonin reuptake inhibitor (SSRI) {e.g., Fluoxetine, Escitalopram, Sertraline}, Serotonin noradrenaline reuptake inhibitor (SNRI) {e.g., Venlafaxine, Desvenlafaxine, Duloxetine} (11). With newer antidepressant drugs like Norepinephrine dopamine reuptake inhibitors (NDRI) {e.g.: Bupropion}, Noradrenergic & Specific Serotonergic Antidepressant (NSSA) {e.g., Mirtazapine} Serotonin Partial Agonist Reuptake Inhibitor (SPARI) {e.g.: Vilazodone} (12). The treatment plan is tailored according to the severity of symptoms, individual patient preferences, and the presence of any comorbid conditions. In conclusion, it is important to understand that Cushing's syndrome-related depression arises due to a specific hormonal imbalance, while MDD includes a broader spectrum of mental health disorders that can occur simultaneously with other medical conditions. Accurate diagnosis and appropriate treatment modalities and consultation with a qualified healthcare professional are important.

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