



Overview On Substance-Induced Mood Disorders

Najlaa Mohammad Alsudairy ¹, Ibrahim Abdullah Almuqrin ², Abdulrahman Ali Shukr ³, Manal Manajaa Alotaibi ⁴, Asma Ahmed Hassan Alghamdi ⁵, Wajdi Ibarahim Abbas ⁶, Joraid, Hussam Abdullah A ⁷, Alanazi Abdullah Tban M ⁸, Abdullah Mohammedhussain ⁹, Mohammed Ibrahim Alsaeed ¹⁰, Dimah Mohammed A Abu Murad ¹¹, Al Sharyah, Salem Mohammed S ¹² And Turki Abdullah Aldalaan ¹³

¹Assistant Consultant FM, National Guard Hospital, King Abdulaziz Medical City, SCOHS, Jeddah, Saudi Arabia. SCFHS Number: I4JM0032715

²PHC Al Salmaniyyah

³General practitioner (GP), Bab Almajeedi Seasonal Health Center

⁴Medical Intern, Imam Muhammad ibn saud Islamic university

⁵Graduate, Princess nourah bent abdulrahman university

⁶Medical Intern, Jazan University

⁷General Practitioner, Health Surveillance Centre

⁸General practitioner, Eradah complex for mental health (ECMH - NB)

⁹General practitioner, Ministry of health

¹⁰King Abdulaziz hospital – AlAhsa

¹¹Medical Intern, Tabuk university

¹²Medical Intern, Najran university

¹³General practitioner, Al-nakheel medical center

Abstract: Despite the fact that both illegal drugs and iatrogenic pharmaceuticals are taken with the intention of improving mood, a sizeable percentage of patients actually have paradoxical affective problems as a result of taking those prescriptions. Some people have manic or depressive episodes instead of the banal bliss that comes with drinking or the "hangover" the next day. Substance-induced mood disorders are those that only manifest in conjunction with substance use. Bipolar disorder and its related disorders, as well as depressive disorders, are examples of affective disorders that can develop in the context of substance use. Previously, these diseases may be found in the DSM-nosological IV's category of substance-induced mood disorders. However, "substance-induced" is now a qualifier for mood disorders in the most recent DSM. In the general population, substance use disorders (SUDs) and depression and bipolar illness usually co-occur. The aim of this review is discussing substance-induced depressive disorder, substance-induced bipolar disorder, and related diseases. It will also go into further detail on how to tell them apart from mood disorders that co-occur with SUDs. Although it is no longer a separate category in the DSM-V, the term "substance-induced mood disorders" will be used to refer to both substance-induced depression and bipolar disorders for the purposes of this review. And the main objective is to collect research and review articles using trusted data base.

Keywords: Mood Disorders, Medication, Drug, Mental Disorders and Depressive

*Corresponding Author

Najlaa Mohammad Alsudairy , Assistant Consultant
FM, National Guard Hospital, King Abdulaziz
Medical City, SCOHS, Jeddah, Saudi Arabia. SCFHS
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I. INTRODUCTION

Although both illegal drugs and iatrogenic pharmaceuticals are used with the intention of improving mood, a sizeable percentage of patients develop paradoxical affective problems after ingesting these treatments. Some people experience a more extreme form of euphoria, such as manic or depressive episodes, as opposed to the more typical euphoria that comes with drinking or the "hangover" the next day. The term "substance-induced" refers to mood disorders that only manifest in connection with substance usage. Both bipolar and associated disorders as well as depressive disorders are affective conditions that can erupt in the context of substance abuse. In the DSM-IV, these diseases were previously identified as belonging to the nosological group of substance-induced mood disorders. But the term "substance-induced" is now used to define mood disorders in the DSM as it stands today. Both depression and bipolar illness are common in the population and frequently co-occur with substance use disorders (SUDs).^{1,2} Treatment of co-occurring mood disorders in patients may lessen cravings and substance use and significantly improve results. When substance use disorders (SUDs) and psychiatric syndromes co-occur, there are at least four major difficulties that could cause difficulty with the diagnosis process.^{3,5} First off, combining SUDs with psychiatric disorders may signify two or more separate problems, each of which is likely to have a distinctive therapeutic pathway.⁶ Second, the first disorder may have an impact on how the second condition develops in such a way that the second disorder then takes a different path. The diagnostic issue of separating affective disorder symptoms from withdrawal and intoxication symptoms from substances can be made easier with a rigorous, stepwise screening and assessment.⁷ The use of psychotherapeutic therapies in treatment should be maximised, and drugs that have been shown to be beneficial in the context of co-occurring substance dependence should be given first consideration. Disorders caused by substances might emerge during either withdrawal or intoxication. Nearly half of the depressive episodes that affect the general population are brought on by alcohol consumption.^{8,10} Cocaine and opiates, particularly heroin, are the second most commonly mentioned substances. Pathological emotional states can also be brought on by iatrogenic drugs. Interferon (IFN), corticosteroids, digoxin, and antiepileptic medicines are a few examples of such pharmaceuticals.^{11,12} Depression can be brought on by either category of substance or medication. According to current theories, the above mentioned drugs change neurotransmitter transmission in significant neuronal circuits such the Papez circuit and mesolimbic tract.¹³

1.1 Pathophysiology

Discussions about the pathophysiology of illnesses induced by substances are still going strong. Changes in cerebral regions such the frontal cortex, nucleus accumbens, olfactory tubercle, hippocampus, amygdala, and hypothalamus are triggered by drug-induced mood disorders.¹⁴ Serotonergic, dopaminergic, corticotropin-releasing factor (CRF), and neuropeptide Y (NPY) neurotransmitter activity changes are all symptoms that contribute to drug-induced mood disorders.^{15,16}

1.2 Epidemiology

The lifetime prevalence of substance-induced depressive disorders is currently estimated to range between 0.26 percent and 1 percent.¹⁷ An estimated 40–60% of people with alcohol use disorders suffer from drug-induced depression.^{18,19} According to data acquired from opioid use disorder outpatient individuals, about 55% of these people had depression brought on by their use of drugs. 16.5 percent and 18 percent, respectively, of those who suffer from serious depression also struggle with alcohol or drug use. Moreover, statistics show that 61 percent of bipolar individuals have a lifetime prevalence of substance use problems.^{20,21} The complexity of the diagnostic problems at the intersection of mood disorders and SUDs is one factor contributing to the variations in reported prevalence rates. Detoxification from narcotics, for instance, can momentarily lower mood, so a patient who is assessed while going through withdrawal may be incorrectly classified as having a mood disorder. Depending on when they conduct assessments in relation to the patient's start of therapy, clinicians may come to different findings.

1.3 Etiology

Disorders caused by substances might emerge during either withdrawal or intoxication. Nearly half of the depressive episodes that affect the general population are brought on by binge drinking.^{8,9,10} Cocaine and opiates, particularly heroin, are the second most commonly mentioned narcotics. Pathological emotional states can also be brought on by iatrogenic drugs. Interferon (IFN), corticosteroids, digoxin, and antiepileptic medicines are a few examples of such pharmaceuticals.^{11,12} Mania or sadness can be brought on by either category of substance or medication. According to current theories, the aforementioned drugs change neurotransmitter transmission in significant neuronal circuits such the Papez circuit and mesolimbic tract.⁷ Recent research has also shown that genes influence the risk of both mood disorders and substance use disorders.¹⁷

1.4 History and Physical

Patients with substance-induced affective disorders will display symptoms that are similar to those of patients with independent mood disorders, whether they also have comorbid substance use disorders or not. Patients may exhibit depressive symptoms such as sadness, sleeplessness, guilt, suicidal thoughts, psychomotor slowness, distractibility, hopelessness, helplessness, irritability, decreased libido, anorexia, or energy. Grandiosity, distractibility, impulsivity, pressured speech, racing thoughts, sexual promiscuity, irritability, sleeplessness, and heightened energy are all signs of mania in the patient. Anamnesis of a patient with a substance-induced affective illness will include mood symptoms that are directly related to the substance's consumption. Following the cessation of acute withdrawal or severe intoxication, these symptoms will go away (up to 1 month). Normal signs of extreme intoxication are those of mania or hypomania, whereas those of withdrawal are those of depression. Alcohol, sedative-hypnotic drugs, analgesics, and other depressants can all cause euphoric feelings, reduced impulse control, and mood instability. The withdrawal phase follows this intoxication period and is characterized by irritability, agitation, and dysphoria. Because stimulant use (such as cocaine, amphetamines, etc.) causes euphoria, increased energy, anorexia, grandiosity, and paranoia, it might mimic bipolar spectrum diseases. Withdrawal from stimulants can result in anhedonia, apathy, depression, and suicidal thoughts.⁷

1.5 Diagnostic Challenges

Understanding of the connections between mood disorders and SUDs has been hampered by ongoing debate over diagnosis. Misdiagnosis of mood disturbance in the context of ongoing substance addiction is a serious worry given the lack of confirmed clinical biomarkers for either MDD or bipolar illnesses.²⁷ It is well known that emotional symptoms are frequent in individuals who are substance-dependent and under treatment, but they frequently change or go away over time with increasing abstinence.^{28,29} This observation makes it more difficult to diagnose MDD and bipolar disorders in patients with SUDs who are actively abusing substances at the time of assessment. This observation is compounded by the fact that intoxication and/or withdrawal from alcohol and other drugs of abuse can cause states that mimic symptoms of independent mood disorders.^{30,31} Since it has been demonstrated that individuals with SUDs both over-³¹ and underdiagnosed mood disorders, it is crucial to distinguish between independent (primary) and substance-induced (secondary) mood disorders.^{32,33} In order to evaluate whether and to what extent mood symptoms are caused by substance use, pharmacologic treatment for depression is traditionally withheld for a period of time once abstinence is achieved. In accordance with the DSM-IV course specified for early full remission from substance dependency and as specified in DSM-IV Criterion C for Substance-Induced Mood Disorder, treatment delays are typically at least one-month long.³⁴ Delaying therapy for mood disorders can unfortunately be troublesome for a variety of reasons. Initially, patients might not be able to start or maintain abstinence for a month or more. Because withdrawal symptoms from substances like alcohol or benzodiazepines can be fatal, establishing abstinence may call for medically supervised inpatient detoxification. Depending on the severity of withdrawal, this usually only takes a short period of time in acute care settings, but after discharge, patients frequently return to their homes, where there is a high chance of relapse within the first 30 days. For instance, Kiefer and colleagues discovered that 65% of untreated participants had ingested alcohol after inpatient detoxification (which is normally much longer in Europe than the US), and 50% had reverted to excessive drinking within 2 weeks of discharge. Untreated depression puts patients at greater risk of relapsing into drinking or drug use, and they do so more quickly.³⁵ Greenfield and colleagues discovered that a diagnosis of major depression at the beginning of inpatient treatment was associated with a shorter time to the first drink (38 days vs. 125 days) as well as a shorter time to a full relapse (41 days vs. 150 days) compared with patients without major depression at admission.³⁶ These findings were made in a cohort of patients hospitalized for alcohol dependence who were followed monthly for a year after discharge. Furthermore, when depressed alcohol-dependent patients were released from treatment without receiving antidepressants, they were more likely to start drinking again than their counterparts who received antidepressant treatment.³⁶ In contrast to those depressive patients who were discharged on antidepressants, 20% of those depressed patients who were discharged on antidepressants had not relapsed after 100 days. It's interesting to note that there were no statistically significant differences between depressed participants who were initially diagnosed with independent MDD and those who were diagnosed with substance-induced depression in terms of the time to first drink or relapse. On the other hand, a lot of people who have underlying alcoholism

or other drug addiction issues see their primary care physician or a mental health specialist complaining of depression, anxiety, or insomnia. Again, a thorough history of alcohol and drug use is essential, but as the majority of doctors are aware, many patients will not disclose truthful information about their drinking and drug use, which lowers diagnostic accuracy. Thankfully, in this situation, laboratory testing like urine drug screens and urine/serum indicators of alcohol consumption can be beneficial in making the right diagnosis. There are three tests that can be used to determine recent alcohol use: urinary ethylglucuronide (EtG), moderate to heavy use (phosphatidyl ethanol), and heavy harmful use (carbohydrate deficient transferrin [%CDT]). While this is outside the scope of this review, suffice it to say that these tests are useful to establish any recent alcohol use. Readers are referred to Litten and colleagues' important review of this subject³⁷. In addition to these laboratory tools, clinicians should be suspicious of alcohol or drug abuse as the underlying cause of psychiatric complaints if any of the following conditions exist: there is a history of substance abuse, there is a family history of substance abuse, there are coexisting or previous medical disorders linked to alcohol or substance abuse (e.g., GI conditions, trauma, HIV, HCV, macrocytic anemia, high uric acid and smoking, There are reports of chronic pain, many relationship issues, several employment changes, and legal issues like DUI arrests, charges of public intoxication, and assault arrests, including domestic abuse.

1.6 High Co-Occurrence of Substance Abuse and Mood Disorders

To explain the significant co-occurrence of substance addiction and mood disorders, several explanations have been put forth. They can be divided generally into three groups. Disorder Fostering Disorder: According to one theory, a mood disorder or SUD may raise the risk for the other by having pathological effects. For instance, those who suffer from mood problems may turn to drugs and alcohol as a coping mechanism. Such an explanation would fit with clinicians' daily observations of people with SUDs claiming to use alcohol and drugs to manage undesirable feelings. Although the drugs may initially lessen or reduce the symptoms of mood disorders, withdrawal and persistent abuse usually make them worse, which breeds more abuse and eventually dependence. According to the self-medication theory, people have a tendency to choose medications that treat their particular psychiatric symptoms. For instance, according to some psychologists, persons with uncontrollable aggression and violence may pick opiates for these drugs' mellowing effects, whereas others who are depressed may select cocaine for its energizing and exhilarating benefits. The evidence supporting the self-medication concept would be strengthened by studies demonstrating such relationships between abusers' preferred substances and their psychiatric diagnoses or symptoms, but few have been reported to date²². Overlapping Neurobiological Pathways: The idea of "kindling" is another theory put forth to explain the high occurrence of comorbidity between mood disorders and SUDs. The phrase, which is typically used in reference to epilepsy, describes the idea that frequent disruptions, such those seen during seizures, sensitize brain tissue. Since it takes less disruption to make neurons more sensitive, untreated epileptic seizures tend to get worse and more frequent with time. Both cocaine and alcohol make neurons more sensitive, and this heightened sensitivity may help explain how both drugs are typically used in a progression from occasional to increasingly frequent and intense use.

There is evidence that mood disorders may also intensify through a kindling process since they frequently follow a similar pattern of progressively more severe symptomatic episodes and progressively shorter intervals of remission. The underlying neurobiological predisposition to sensitization in susceptible individuals may therefore develop both drug dependency and mood problems, according to the kindling theory for comorbidity²³. Underlying Genetic Factors: Genetic risk factors exist for both substances abuse and mood disorders, according to research. Additionally, families with substance abusers are more likely to have members with mood problems than families without, and the opposite is true. The likelihood that some gene variations may increase the risk for both types of sickness is raised by these facts. The genes of a person could: predispose him or her susceptible to mood problems, for which he or she may subsequently attempt self-medication, change the brain so that it reacts to first-time drug exposures in a way that encourages chronic substance usage, and the drugs subsequently cause changes in the brain that result in mood disorders; lead the brain to develop in a way that specifically promotes both disorders, such as by making the brain more susceptible to neuronal sensitization and kindling.

1.7 Evaluation

The mood disorder brought on by drugs will resemble the relevant independent affective disorder. As a result, drug-induced depression will adhere to diagnostic standards for assessing depressive illnesses, and drug-induced bipolar disorder will mimic conditions on the bipolar spectrum. As suggested by the label "substance-induced," a true diagnosis requires either admission of substance consumption or a positive lab test. The most straightforward characteristic to distinguish between a substance-induced and independent emotional illness is temporality. As previously stated, symptoms of a substance-induced mood disorder will go away once acute withdrawal or severe intoxication has stopped (up to 1 month). A low mood or a noticeably decreased interest or enjoyment in all aspects of life describe the clinical picture of substance-induced depressive disorder, and the symptoms are supported by the history, physical examination, or test results. A noticeably lessened interest or pleasure in many aspects of life, as well as an inflated, expanded, or irritated mood, with or without a sad mood, characterize the clinical picture of substance- or medication-induced bipolar. The narrative, physical examination, or test results support the clinical evidence. Other causes of the persistent affective illness should be ruled out by laboratory and imaging data, along with a thorough history.²¹

1.8 Course of Illness and Prognosis

All medical practice relies on the interrelationships of diagnosis, prevalence, illness course, and therapy, but they are crucial in the context of psychiatric comorbidity. The prognosis of a particular person and the creation of a treatment plan both depend on an accurate diagnosis.^{38,39} As individuals with the disorder(s) are longitudinally monitored and treated over time, understanding the natural history of a specific disease and its expected reaction to treatment may help in accurately identifying it.⁴⁰ For instance, it is realistic to assume large rates of mood episodes that are mostly or completely related to substance use and that do not reoccur unless active substance use is restarted, given the high frequency of both SUDs and depression. However, neither

clinical samples nor epidemiological research have shown that this is always the case. Ramsey et al., for example, discovered that over 25% of treatment-seeking alcoholics who were initially diagnosed with SIMD at baseline were later reclassified as having MDD throughout the course of the subsequent year of follow-up. Similar to this, Nunes and colleagues found that 57% of inpatients with cocaine, alcohol, or opioid dependence who were monitored for a year after release fulfilled DSM-IV criteria for a severe depressive episode. Only 14% of depressed patients were categorized as having SIMD during follow-up, compared to the initial 51% of the sample who had SIMD at admission. Patients who were initially diagnosed with substance-induced depression at baseline were equally likely to experience a major depressive episode during follow-up as those who were initially diagnosed with MDD; in the overall group of depressed patients, the mean number of weeks experienced depressive symptoms over a 12-month period was 25.6. (SD 15.3). This question can be answered in a nonclinical sample of more than 2000 respondents who satisfied lifetime criteria for MDD and SUD at Wave 1 thanks to recent analysis of data from NESARC's Wave 2, which was done roughly 3 years after the first survey. Only 0.26% of depressed respondents with SUDs, or 106 respondents, were identified as having SIMD in Wave 1. Of these, 88 were resurveyed in Wave 2, and 95% of these individuals were reclassified as having MDD^{38,39}. Despite the high frequency of co-occurring mood disorders and SUDs, there is a paucity of prospective research identifying prognostic variables for either mood or substance use outcomes. Other researchers have pointed out that the spacing between follow-up visits in these studies tended to be long and quite variable, and that actual amounts of substance intake received little to no attention.^{41,42} The majority of early prospective studies found that substance abuse was associated with increased syndromal mood recurrence and shorter time in remission in bipolar disorders⁴³. Future study findings have been inconsistent. In the New Hampshire Dual Diagnosis Study, 51 patients with bipolar disorder and comorbid SUDs underwent a 3-year course that was marked by significant improvement in functional status and substance abuse outcomes (61% in full remission at 3 years), but only modest improvement in bipolar symptoms, with weak relationships among outcome domains.⁴⁴ In contrast, a sample of bipolar drinkers who were prospectively observed for a year by van Zaane and colleagues revealed significant variation in alcohol use with no discernible connection with mental symptoms or functional status. In more recent research, Farrer and colleagues observed that in alcohol-dependent patients with MDD or bipolar illness who were monitored over a 5-year period, drinking outcomes improved and depression intensity generally decreased (as did mania severity in bipolar alcoholics)⁴⁵. This research team discovered that there was no relationship between the severity of either depression or mania, as determined by the Beck Depression Inventory (BDI) or the Young Mania Rating Scale (YMRS), and the number of abstinence days or drinking days at 5 years, but that the BDI and YMRS scores were positively correlated with the amount of alcohol consumed each drinking day. In this cohort, drinking results at 5 years were most accurately predicted by drinking outcomes at earlier time points, while age, gender, or mood diagnosis were not related to drinking outcomes⁴⁵. In conclusion, the connection between the various illness courses of co-occurring mood disorders and SUDs seems to be complicated and understudied at this time. As a result, it could be a good idea to think twice before making generalizations about how certain people or clinical groups as a whole are affected by the

interaction between mood and substance use problems. Given the clear therapy implications, much more research on disease progression is necessary.

1.9 Substance Misuse

Of all mental health problems, bipolar disorders have the highest prevalence of substance abuse (Ladson et al., 2014). At some point in their lives, between 48 to 61% of people with bipolar disorder will develop a substance use disorder (Ladson et al., 2014). Those who have bipolar disorder and utilize drugs concurrently suffer unfavorable effects. Concurrent substance use and bipolar disorder are associated with an earlier onset of the disorder, an increase in suicide attempts, an increase in completed suicides, more severe manic and depressive episodes, more mixed and cycling episodes, worse physical health, worse psychosocial functioning, and higher rates of treatment non-adherence. It might be challenging to distinguish between substance use and bipolar disorder symptoms. Both substance use disorders and bipolar I disorder share symptoms like hyper arousal, weight loss, diminished impulse control, sleeplessness or decreased need for sleep, and psychotic characteristics. Some substances, like methamphetamine and cocaine, can cause intoxication and withdrawal symptoms that resemble both manic and depressed symptoms. Mood fluctuations can be momentarily concealed by narcotics, alcohol, and other drugs like marijuana. When bipolar disorder is mistaken for unipolar depression or another mental illness, affected individuals may self-medicate with drugs. The existence of a substance use disorder complicates the treatment of bipolar disorder, and the presence of a bipolar disorder can complicate the treatment of a substance use disorder. Mania's impulsivity and poor judgment might lead people to participate in high-risk behaviors such as drug or alcohol use when they might not have otherwise. Alcohol or narcotics may be used by those going through a depressed episode to ease their symptoms. Some psychiatric drugs may worsen symptoms or raise the danger of an overdose when combined with non-prescription pharmaceuticals or illegal substances. Both illnesses must be precisely identified and treated for treatment to be effective. Referral to a facility that specializes in treating substance use and mental health issues concurrently may be necessary due to the difficulties in treating clients with co-occurring substance use and bipolar illnesses.⁴⁶

1.10 Facts and Figures

Worldwide, 45 million people suffer from bipolar disorders (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018). According to Marsh (2022a), bipolar disorder I has a lifetime prevalence rate of 1.0-1.6%, while bipolar disorder II has a lifetime prevalence rate of 0.5-1.0%. (Marsh, 2022b). Bipolar disorder occurs in 1-2% of children and adolescents (Birmaher, 2013). There don't seem to be any racial disparities in the prevalence of bipolar disorders. Males and females both experience bipolar I, although females are more likely to experience rapid cycling and bipolar II. The average age at which bipolar disorder manifests itself is 25. (Yatham et al., 2018). The misdiagnosis of bipolar disorder frequently causes a delay in treatment after the start of symptoms. 35% of these persons did not receive an accurate diagnosis for ten or more years after they first sought therapy; 69% of adults whose bipolar disorder was ultimately correctly identified had their condition initially misdiagnosed (Ladson et al., 2014). The average time it takes for a kid or adolescent to

receive a correct diagnosis is more than 16 years (Ladson et al., 2014). When suffering mania or hypomania, people with bipolar disorder are less inclined to seek therapy; when depressed, they are more likely to do so (NIH, 2020). 60% of people with bipolar illness will experience a relapse within two years, and 27% of those with the condition will experience another episode of mania or depression within a year, even with medication (Geddes & Miklowitz, 2013). In 2018, it was projected that bipolar illness cost the US economy \$195 billion, with direct healthcare expenditures accounting for 25% of the total (Bessonova et al., 2020). In the United Kingdom, the economic costs of bipolar disorder were estimated to be \$6.43 billion in 2018–2019, with lost productivity and informal care accounting for 68% of these costs, healthcare costs accounting for 31%, out-of-pocket costs representing 1%, and social care expenses representing 0.5%. (Simon et al., 2021).⁴⁶

1.11 Risk Factors

One of the most heritable mental health conditions is bipolar disorder, which is thought to be caused by a mix of genetic predisposition and significant stresses in life (Marsh, 2022a). First-degree relatives are ten times more likely to acquire bipolar disorder if there is a family history of the condition (Boland et al., 2022). Given that a family history of schizophrenia significantly raises risk, bipolar illness and schizophrenia are probably genetically connected. In people with bipolar disorder, a stressful event like a death in the family, a divorce, or money troubles may set off a depressed or manic episode. Another risk factor for bipolar disorder is substance addiction. People with bipolar disorder are more likely than the general population to have medical issues like obesity and cardiovascular disease (Miller et al., 2015). The risk of substance use and impulsivity associated with manic episodes is increased.⁴⁶

1.12 Clinical Presentation

Mania, hypomania, and/or depressive episodes will occur in people with bipolar disorders. People who are going through a manic episode could seem euphoric, impulsive, impatient, agitated, overly chatty or social, or they might have an inflated sense of their own importance or have less need for sleep. A hypomanic episode may cause some of the same symptoms as mania, although to a lower extent. People who are depressed may exhibit symptoms such as a loss of interest in routine activities, exhaustion, excessive sleep or insomnia, low vitality, or impaired mental and bodily functions. It is possible for someone to experience rapid cycling between manic, hypomanic, or depressive episodes, changing their emotional states numerous times in a 24-hour period. Additionally, mixed states can happen when a person exhibits signs of mania, hypomania, or depression all at once.⁴⁶

1.13 Treatment

Psychosocial counseling, typically in a combination of group and individual settings, has historically been the method used to treat SUDs in the United States. The present review will limit the discussion to the current evidence base for pharmacotherapy in patients with co-occurring SUDs and mood disorders, despite advancements in the development of integrated group therapy and the application of well-established behavioral approaches like contingency management⁴⁷. The majority of earlier research has been on the use of antidepressants in patients with MDD and

concomitant SUDs. Prior to the invention of selective serotonin reuptake inhibitors (SSRIs), research and clinical application of tricyclic antidepressants or monoamine oxidase inhibitors in depressed patients with comorbid SUDs were hampered by safety concerns surrounding the possibility of deadly overdose.⁴⁸ Only one third (14 of 44) of studies that were completed at the time that focused on comorbid SUD and mood disorders satisfied the requirements for sufficient placebo-controlled, double-blind, randomized prospective clinical trials, according to Nunes and Levin's 2004 meta-analysis³⁹. Antidepressants may have a modestly beneficial effect on mood symptoms in depressed individuals with SUDs, according to this meta-analysis. However, it also noted that effects across studies were highly heterogeneous, with almost no effects seen on substance use outcomes outside of trials where depression effect sizes were >0.5 . According to Nunes and Levin, extrapolation between antidepressant efficacy and effects on substance use outcomes in these trials, either within or between studies included in the meta-analysis, was prevented by the discovery of a number of moderators of depression outcomes (e.g., placebo response, sample characteristics, time of depression diagnosis, etc.)³⁹. In a review of antidepressant studies in depressed alcoholics, Pettinati reported findings that were similar: 75% of the trials found efficacy for reducing depression symptoms, while only a minority had beneficial effects on drinking outcomes.⁴⁹ It's interesting to note that a large multisite trial of sertraline (50 to 150 mg) involving 345 alcohol-dependent adults with MDD demonstrated no benefit of sertraline over a placebo for either drinking outcomes or depression. It's significant that this experiment used randomization based on the distinction between secondary and independent depression and generally showed no differences depending on this categorization⁵⁰. In a more recent study, Sertraline plus the opioid antagonist Naltrexone, one of three drugs licensed by the FDA to treat alcoholism, significantly reduced drinking in depressed alcohol-dependent people, according to Pettinati and colleagues. For 14 weeks while undergoing weekly cognitive behavioral treatment, patients in this trial were randomized to receive either sertraline, naltrexone, the combination of sertraline and naltrexone, or double placebo. The rate of abstinence in the group receiving the sertraline and naltrexone combination was much higher (53.7%), in fact double that of the comparator groups (21.3% to 27.5%)⁵¹. Additionally, compared to either of the comparison groups, participants in the combo group showed a noticeably longer delay before relapsing to heavy drinking. This result also tended to favor the sertraline + naltrexone combination treatment, even if variations in the improvement of depression scores among groups fell just short of statistical significance. In comparison to the other treatment groups, the combination therapy was well tolerated. The study by Pettinati et al., which suggests treating MDD and alcohol use disorder simultaneously with medications indicated for each condition should be a treatment standard—again emphasizing the need for accurate assessment and diagnosis—is a turning point in dual-diagnosis treatment research that may have an immediate impact on clinical practice. According to Moak et al., sertraline combined with CBT (similar to that used in the Pettinati research) decreased the number of beverages consumed per day compared to placebo and was more effective at lowering depression in women⁵². Even less is known regarding the best course of treatment for patients with bipolar disorder and concurrent SUDs because there have been relatively few randomized controlled drug trials. Only nine clinical trials that used substance use as the key performance indicator in this cohort

have been reported as of this writing.⁵³ In three of these studies, people with bipolar illness and stimulant addiction were tested. Lamotrigine showed promise in treating both conditions, while the dietary supplement citicoline showed promise in treating both methamphetamine and cocaine use as well as bipolar disorder⁵⁴. In fact, the use of any chemical treatments for addiction in general continues to be constrained by the dominant opinion of many treatment professionals, patients, and society at large. As a result, in the United States, the uptake of medication-assisted treatment of SUDs in people with or without mood disorders is still dismally low.⁵⁵ The evidence available suggests that this is particularly true for people who also have co-occurring mood and substance use problems. In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) research, for instance, just 0.4% of the vast number of bipolar patients with SUDs who were recruited were receiving approved pharmacological therapies for alcohol or heroin dependency⁵⁶. Similarly, people with bipolar disorder frequently smoke cigarettes and make little attempts to quit, but few psychiatrists bring up the topic with their patients, and even fewer combine counseling with proven methods for treating nicotine dependence^{57,58}. It is implied by the diagnosis of substance-induced mood disorder that the disorder should go away on its own once the aggravating factor has subsided. However, depending on how severe a substance-induced emotional episode is, medication may be required. The clinician's choice of whether to treat the active affective disorder or just provide supportive care while monitoring the patient in a secure environment during the withdrawal period will be aided by clinical judgment, supported by a proper history and collateral information. Some studies advise the empiric use of antidepressants in the presence of depressed symptomatology and concurrent substance use due to the relative safety of the majority of antidepressants²¹. Second-generation antipsychotics, including quetiapine or olanzapine, are advised by guidelines because they act more quickly than mood stabilizers during manic episodes.^{24,26} The focus on abstinence from the triggering substance should be the most important aspect of treatment. Depending on the patient's preferred substance, the treatment method will change.

1.14 Complications

Suicide is the biggest issue that surrounds substance-induced mood disorders. Studies show that substance-induced emotional problems are more frequently associated with suicide attempts. According to one study, there is an almost four-fold greater risk of suicide attempts when a mood disorder coexists with substance abuse.⁵⁹

1.15 Deterrence and Patient Education

- Avoid using alcohol or illegal substances.
- Avoid the environment or individuals who are most likely to cause you to use alcohol or illegal drugs.
- To aid in the healing process following alcohol and drug usage, take into account psychosocial interventions like AA and NA.
- Any new medicine recommended by another doctor should be discussed with a doctor because some medications can lead to mania or depression.
- If you have questions about over-the-counter medications, speak with a doctor right away because some OTCs may intensify the effects of other prescriptions and even result in mania or depression.

- Limit your coffee intake, stop smoking, and eat a balanced diet.
- Be mindful of any episodes of mania or depression that follow the start of substance use or prescription usage, and talk to your primary care physician or psychiatrist about them.⁶⁰

1.16 Enhancing Healthcare Team Outcomes

- A multidisciplinary strategy comprising the patient, the patient's family, the doctor, the nurse, and the therapist is necessary to manage substance-induced disorders. Although substance-induced diseases (depression and bipolar) go away after the biological effects of the drug wear off, psychological and medical repercussions can be fatal in vulnerable persons who acquire full-blown major depressive disorder or bipolar disorder.
- Doctors and designated nurses at the emergency room are in charge of organising the following types of care:
 - Drug concentrations in the blood or urine.
 - Keep an eye out for any respiratory depression or cardiac arrhythmias in the patient.
 - For acute mania, provide benzodiazepines or antipsychotics.
 - to rule out rhabdomyolysis, use creatine phosphokinase (CPK).
 - Rehydrate the patient with sterile saline.
 - Give 1:1 to ensure safety (suicide and injury to others).
 - When there are immediate dangers to oneself or others, consider involuntary status.
 - As a last resort, physical constraints.
 - Speak with an expert on addiction.
 - In the outpatient clinic, the doctor and the designated nurse are in charge of:
 - In cases of extreme mania or severe depression, ensure the patient's safety and the safety of others.
 - The patient is transported to the emergency room.
 - If you pose an immediate threat to yourself or others, think about being committed involuntarily to a mental health facility.
 - The family should be discussed with and included in the treatment plan by the doctor, the nurse, and the therapist.

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- The finest results can be attained with the aid of an interprofessional team that offers a comprehensive and integrated strategy.⁶⁰

2. CONCLUSION

SUD and affective disorders frequently co-occur, which has an effect on therapy and prognosis. Because the symptoms of substance use disorders, withdrawal, and mood disorders substantially overlap, diagnosing and assessing these comorbid diseases is challenging. For busy practitioners, using screening tools to identify people who may have mood problems and then following up after a period of abstinence may be a particularly useful strategy. Manuals for several treatment philosophies that have been created especially for people with SUD, depression, or bipolar disorder are available. Even though some community treatment settings might not be appropriate for the use of complicated manual-guided therapies, these research and others that are now underway should establish the essential elements and methods of effective therapy for these patients. There is still need for research on the optimal strategy for putting these treatments into practice.

3. AUTHOR CONTRIBUTION STATEMENTS

Authors who collected the data

Najlaa Mohammad Alsudairy , Ibrahim Abdullah Almuqrin , Abdulrahman Ali Shukr, Manal Manajaa Alotaibi.

Authors who wrote the manuscript

Asma Ahmed Hassan Alghamdi, Wajdi Ibarahim Abbas, Sjoiraid, Hussam Abdullah A, Alanazi Abdullah Tban M.

Authors who reviewed and checked

Abdullah Mohammed Hussain , Mohammed Ibrahim Alsaeed , Dimah Mohammed A Abu Murad, Al Sharyah, Salem Mohammed S , turki abdullah aldalaan.

4. CONFLICT OF INTEREST

Conflict of interest declared none.

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