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ASSOCIATION OF ALCOHOL USE DISORDERS (AUD) AND PSYCHIATRIC MORBIDITIES AND THEIR TREATMENT MODALITIES

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ABSTRACT: The prevalence of psychiatric disorders in AUD, the association between the severity of AUD and psychiatric disease, the influence of treatment of AUD on relief of psychiatric symptoms and vice-versa has been studied in various parts of the world. In India, the influence of various socio-economic factors and the lifestyle of the individuals is different to other parts of the world. There is paucity of the literature regarding the association of AUD with psychiatric disease, influence of AUD on pharmacotherapy of psychiatric disorders, the quality of life of patients with co-existing AUD and psychiatric disorders. This review aims to study the association and co-occurrence of AUD and psychiatric disorders and influence of combined disorders on the treatment.

INTRODUCTION: Alcohol use disorder (AUD) is a medical condition characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. It encompasses the conditions that some people refer to as alcohol abuse, alcohol dependence, alcohol addiction, or alcoholism [1]. AUD is considered as a brain disorder. The three major risk factors for AUD are consumption of alcohol at an early age, genetics and family history of alcoholism, and a wide range of mental health conditions [1]. The spectrum of AUDs can be mild, moderate and severe. Effective and timely screening of alcohol use can be used to control the extent of alcoholism [2].

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Alcohol and the Brain: Alcohol alters the neurotransmitters such as gamma amino butyric acid (GABA), dopamine, and glutamate. The effects of GABA are first amplified by alcohol (i.e., it increases inhibition, and often the brain becomes moderately drowsy). Long-term, heavy alcohol usage, however, eventually lowers the total number of GABA receptors. Reduced inhibition along with a GABA receptor deficit may increase brain over excitation when an individual stops drinking. Withdrawal seizures may then follow within a day or two of these [3].

The amino acids aspartate and glutamate are the main excitatory neurotransmitters in the brain. They function through a combination of non-NMDA and NMDA receptors. Both NMDA and non-NMDA receptor activity is inhibited by brief exposure to intoxicating alcohol concentrations, which may lead to drowsiness initially. After long term exposure, brain decreases inhibitory neurotransmission and enhances excitatory

neurotransmission [4]. Alcohol affects various brain regions like frontal cortex, hippocampus, cerebellum and limbic system affecting decision making, memory function, coordination and emotional balance respectively altering mood, cognition, and behavior [5]. Patients with cerebral hemisphere damage on the left side typically experience language difficulties, whereas those on the right side typically struggle with nonlinguistic things like music, designs, maps, and other visual arts and may even exhibit emotional indifference [5].

Numerous factors like patient's age, gender, literacy status, genetic background, and family history of alcoholism and also the quantity, timing, and duration of alcohol consumption influence the effects of alcoholism on the brain [6, 7]. Apart from that coexisting medical, neurological, and psychiatric disorders can exacerbate the effects of alcoholism on the brain and behavior [7, 8].

Alcohol use Disorder (AUD): Alcohol use disorder (AUD) is a diagnostic term used to describe a chronic pattern of alcohol misuse that leads to significant impairment or distress [1]. It is characterized by a problematic pattern of alcohol consumption that includes symptoms such as loss of control over drinking, continued use despite negative consequences, and a strong desire or craving to drink [1]. AUD is a clinical diagnosis that is based on specific criteria like the amount and frequency of alcohol consumption, the presence of withdrawal symptoms when alcohol use is stopped or reduced, and the impact of alcohol use on daily functioning and relationships, as outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [8]. According to DSM-5 alcohol abuse and dependence aremerged into a single diagnosis of mild, moderate, or severe AUD. AUD is a serious condition that can have significant physical, psychological, and social consequences. Treatment for AUD typically involves a combination of behavioral therapies, medications, and support groups [8].

Alcohol use Disorder and Neuropsychiatry: Alcohol use disorder (AUD) has been found to be associated with all the neuropsychiatric disorders [9]. The interaction between AUD and psychiatric disorders has complicated the diagnosis and treatment of the other disorder. Some of the common psychiatric conditions associated with AUD are depression, anxiety, bipolar disorders, schizophrenia, attention deficit hyperactivity disorder (ADHD), borderline and antisocial personality disorder, eating disorders [10, 11].

Co-occurrence of AUD & Psychiatric Disorders and their Treatment: A systematic review and meta-analysis by Puddephatt *et al* which included 3,82,201 patients, reported 32.5% global incidence of alcohol consumption and 5.1% global incidence of AUD [10]. Major depressive disorder is the most prevalent mental illness, affecting 10% to 15% of people at some point of their life [12, 13]. The global incidence of depression and anxiety were reported as 4.4 and 3.6% respectively [10].

Amongst all the psychiatric disorders, depression is most commonly associated with alcohol abuse. People with DSM-IV alcohol dependence are 3.7 times more likely to also have major depressive disorder, and 2.8 times more likely to have dysthymia [14]. Particularly, people with DSM-IV AUD are 2.3 times more likely to have experienced severe depressive illness than people without AUD [15]. The associations between CMD and AUD were stronger for moderate or severe AUD (12% prevalence) compared to mild AUD (7% prevalence) [10].

According to some studies, AUD precedes depressive disorders [16]. The symptoms of alcohol abuse may be primarily responsible for the causative connections between AAD and MD, as rates of alcohol abuse were greater than those of alcohol dependence [17]. Studies have indicated a link between the occurrence of depressive symptoms and problems in teenagers who drink heavily or regularly [17]. The results of a meta-analysis showed that the common mental disorders (depression, anxiety, and phobia) had a twofold increase in the odds of reporting an AUD with odds ratio of 2.02 [12].

Almost 33% of persons in treatment for DSM-IV AUD met criteria for major depressive disorder in the past year, whereas 11% met criteria for dysthymia. Disulfiram and naltrexone are safe drugs for patients with dual diagnosis of depression and alcohol use disorders [7]. Antidepressant-AUD drug combinations (such as sertraline plus

naltrexone or acamprosate plus escitalopram) have demonstrated some potential in treating these co-occurring illnesses, with good results for depression symptoms as well as AUD [18, 19].

The results of a Cochrane database review that included 14 studies and 1074 participants showed that antidepressants, compared to placebo, reduced the severity of depression compared to that of a placebo, this evaluation was done using scales and calculated at the end of trial [20]. According to some more studies with very low-quality evidence, antidepressants were effective in increasing the response to the treatment (10 studies, 805 participants with risk ratio (RR) 1.40 and according to Moderate-quality evidence, antidepressants increased abstinence from alcohol during the trial (7 studies, 424 participants, RR 1.71and reduced the number of drinks per day [20].

A meta-analysis of 123 papers and 1,65,811 participants with schizophrenia revealed a 24.3% prevalence of AUD. Another study found that 36.4% of 404 participants exhibited AUD prior to their first episode of psychosis [21]. An increased chance of co-occurring AUD and schizophrenia can result from genetic factors. Another study found that 18.9% of people with a diagnosis of substance-induced psychosis had alcohol as their major substance [20].

First-generation antipsychotic medications did not appear to decrease alcohol use and actually has increased substance use and craving in people with schizophrenia and co-occurring substance use disorder [22, 23]. Among second generation or atypical antipsychotic medications, clozapine was found to be more effective than other atypical antipsychotics [24]. Other atypical antipsychotics such as “injectable” long acting risperidone or paliperidone were also found to be effective [25, 26, 27]. Participants in a study who were prescribed clozapine as opposed to those who were on another atypical antipsychotic experienced remission from AUD (79% versus 34%) [24]. Compared to individuals treated with other antipsychotics(40%), those in remission who had taken clozapine had a lower rate of relapse to substance use (8%) [24]. Participants receiving clozapine had considerably greater rates of abstinence (54% vs. 13%, p =.05) compared to one receiving risperidone [24].

In a 12-week, randomized controlled trial, 31individuals with schizophrenia and co-occurring alcohol use disorder were treated with naltrexone (50 mg) or placebo, in addition to neuroleptic medication. Participants with naltrexone treatment, had fewer number of drinking days, heavy-drinking days(defined as more than five drinks), and lesser craving compared to those who received placebo [28, 29].

The association between alcohol dependence and anxiety disorders is bidirectional [30, 31], [31]. The results of the study showed that the probability of a person with an anxiety disorder meeting the criteria for alcohol dependency more than doubled (OR = 2.3) as compared to an individual without an anxiety problem. Individuals with alcohol-related illnesses along with co-occurring anxiety or depression respond poorly to treatment [1, 32].

According to Kushner and colleagues, after receiving intensive inpatient therapy for alcohol misuse, more than twice as many participants with co-occurring anxiety or mood disorders compared to those without such disorders returned to any drinking within four months (52% vs. 21%) [1, 33]. In a study by Sarah *et al*, the authors evaluated whether pharmacological treatment with paroxetine for anxiety, reduced the alcohol use and relapse after treatment [34]. In a double blinded study, Paroxetine and a placebo were administered to participants with AUD and social anxiety disorder, while the drug was found to be beneficial in reducing the symptoms of social anxiety, the degree of alcohol consumption remained constant [34, 35].

In another randomized controlled trial, 59 participants with bipolar I disorder, and alcohol dependence received either valproate or placebo and all received usual treatment of Lithium. Compared to the group that received a placebo, the valproate group displayed a trend toward fewer drinks per heavy-drinking day as well as a significantly lower proportion of heavy-drinking days [26, 36]. Individuals with borderline personality disorders and mild psychiatric disease are at increased risk of substance abuse [37]. Psychotherapy has been advised as the primary treatment for borderline personality and antisocial behavior, associated with alcohol use disorder.

Pharmacotherapy has been advised as adjuvant treatment [38]. Atypical antipsychotics medications such as aripiprazole and olanzapine, and atypical antipsychotics topiramate and lamotrigine had been investigated [39].

In another study, administration of Topiramate and lamotrigine resulted in decreased intensity of alcohol consumption, reduced craving for participants who had AUD and decreased anger intensity and reactions for those who had BPD [39]. Aripiprazole and olanzapine reduced anger intensity and impulsiveness, but the reduction in number of drinking days and craving was not consistent [39]. In another study where participants were divided into two groups Type A (less severe alcohol use disorder) and Type B(severe AUD, high levels of dependence), Selective serotonin reuptake inhibitor (SSRI) sertraline, was more effective in reducing the number of drinking days, time to relapse, and continuous abstinence period, for individuals in the Type A compared with those in the Type B group [40].

CONCLUSION: The efficacy of pharmacotherapy for AUDs is well-documented, but there is a need for more research on the treatment of AUDs among psychiatric populations with mood, anxiety, and psychotic disorders [41]. Research suggests that both pharmacological and psychological interventions can be effective in treating alcohol use disorder (AUD) with coexisting psychiatric disorders.

Antidepressants, particularly when combined with anti-alcohol medication, have shown some efficacy in treating comorbid AUD and depressive disorder [7]. Selective serotonin reuptake inhibitors (SSRIs) and other medications have shown promise in treating comorbid AUD and anxiety disorder [42]. For individuals with comorbid post traumatic stress disorder (PTSD) and AUD, Topiramate and Prazosin have shown potential in reducing symptoms [43]. However, more research is needed to further evaluate the efficacy of all these treatments.

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