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CLINICAL ASSESSMENT OF SLEEP QUALITY AND COGNITION IN ALCOHOL DEPENDENCE AND WITHDRAWAL SYNDROMES - A COMPARATIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Alcohol dependence syndrome (ADS) is a chronic disorder characterized by compulsive alcohol use, tolerance, and withdrawal. Long term alcohol consumption disrupts normal sleep patterns, leading to poor sleep quality, reduced sleep duration, and fragmented sleep. These disturbances negatively affect physical and mental health and may increase the risk of relapse. ADS is also associated with cognitive impairment, particularly in memory, attention, and executive functions, due to alcohols neuro toxic effects on the brain. These cognitive deficits can interfere with daily functioning and treatment outcomes. Understanding sleep quality and cognitive changes in ADS patients is essential for early identification and comprehensive management. **Aim:** To assess the sleep quality and cognitive impairment among patients diagnosed with alcohol dependence syndrome using standardized evaluation tools. **Materials And Methods:** A cross-sectional study was conducted over 6 months during the year 2025 to 2026 in the psychiatric department of Andhra Pradesh Vaidya vidya parishad hospital, Proddatur. A total number of 120 alcohol – attributed patients meeting the inclusion criteria were evaluated. **Results:** Overall 120 patients were included in the study. The demographic analysis revealed that 100 % of Male patients are consume Alcohol as a part in their daily life. The study is classified Alcohol induced diseases into two types : Alcohol Dependence Syndrome (ADS) [20% patients are Mild, 54% patients are Moderate, 42% patients are Severe] and Alcohol

Withdrawal Syndrome (AWS) [33% patients are Mild, 33% patients are Moderate, 41% patients are Severe]; Alcohol induced Sleep Abnormality [0.83% patients have Good Sleep, 19.17% patients have Poor Sleep , 38.33 % patients have Moderate Sleep and 41.67% patients have Severe Sleep abnormality] and Cognitive Impairment [30.08% patients have Normal, 43.3 % patients have Mild, 24.39% patients have Moderate and 1.7% patients have Severe Cognitive Impairment] and Comparative Drug Therapy on Lorazepam [15%] and Chlordiazepoxide [40%] were frequently observed. **Conclusion:** Alcohol Dependence Syndrome (ADS) and Alcohol Withdrawal Syndrome (AWS) is strongly associated with significant Sleep disturbances and Cognitive impairment among affected patients. The study showed that most patients had moderate to severe ADS and AWS**.** A large proportion of patients experienced Moderate to Severe sleep abnormalities**,** indicating that chronic alcohol consumption disrupts normal sleep patterns. Cognitive assessment revealed that many patients had mild to moderate Cognitive impairment**,** affecting memory and attention. Chlordiazepoxide was more frequently used than lorazepam in the management of alcohol withdrawal symptoms.

KEYWORDS: Alcohol Dependence Syndrome (ADS), Alcohol Withdrawal Syndrome (AWS), Sleep Impairment, Cognitive Impairment, Lorazepam, Chlordiazepoxide.

INTRODUCTION

ALCOHOL

Alcohol is a chemical compound widely used as a psychoactive substance. It is produced primarily by Fermentation process of Carbohydrates especially Sugars mainly carried out by Yeast. Humans are consuming alcohol as a beverages since over thousands of years ago. The alcohol taken by humans is **ETHANOL** or **ETHYL ALCOHOL**.[1][2]

➢ CHEMISTRY OF ALCOHOL

Alcohols are **Organic chemical compounds** that contain one or more **hydroxyl groups {-OH}** that are attached to a Saturated Carbon atom. The formula of common alcohol (Ethanol) is C2H5OH, elemental composition includes **C**:50-52%, **H**:11-13%, **O**:30-35%.[3]

➢ TYPES OF ALCOHOL[4]

I. LOW ALCOHOL BEVERAGES [ABV: < 3%]

Ex: - Light beer (Brewed and Fermented)

II. MEDIUM ALCOHOL BEVERAGES [ABV: 3 – 15%]

Ex:-Regular beer, Strong beer (Brewed and Fermented), Wine (Fermented).

III. HIGH ALCOHOL BEVERAGES [ABV: 15 – 40 %]

Ex:- Vodka, Rum, Brandy, Whisky, Liquor (Distilled)

IV. VERY HIGH ALCOHOL BEVERAGES [ABV: >40%]

Ex :- Absinthe, Bacardi.

- **KEY DIFFERENCES BETWEEN FERMENTED AND DISTILLED ALCOHOLS**[5][6]

❖ **Fermented alcohols or Fermented beverages** are produced by the fermentation of **Sugars** [Present in grains, fruits etc] along with **Yeast** [mainly by ***Saccharomyces cerevisiae***] those are convert sugars into Ethanol {C_2H_5OH} and Carbon dioxide {CO_2}. Fermented alcohols are usually **Low alcoholic (4-15% ABV)**.

- **Ex:-** Beer (Strong beer, Light beer, Regular beer), Wine etc.

❖ **Distilled alcohols or Distilled spirits** are produced initially by fermenting sugars and followed by Distilling the fermented liquid **(Fermentation + Distillation)** to enhance the Alcohol concentration. Distilled alcohols are usually **High alcoholic (35-50% ABV)**.

- **Ex:-** Whisky, Vodka, Rum, Brandy etc.

- **UNITS OF ALCOHOL** [7] **:-**

1 unit of alcohol = 10 ml or 8g of Ethanol

NOTE

✓ Men shouldn't regularly drink more than 3 to 4 units per day {30- 40 ml}

✓ Women shouldn't regularly drink more than 2 to 3 units per day {20- 30 ml}

Example :- A 300 ml of beer with 5 % of Ethanol :- 300 x 5 / 1000 = 1.50 units

- **QUANTITY OF ALCOHOL**

Table No. 01: Quantity of Alcohol with respect to Types.

SL.NO	TYPES	STANDARD QUANTITY	QUANTITY [in ml]	ABV	UNITS
1	**Beer (Regular)**	1 bottle / 1 glass	330 ml	4-6%	1.3
2	**Strong Beer**	1 bottle	330 ml	6-8%	4

3	**Light Beer**	1 bottle	330 ml	3-4%	1
4	**Wine**	1 standard glass	150 ml	10-15%	1.8
5	**Whisky**	1 peg	30 ml	40-45%	1.2
6	**Brandy**	1 peg	30 ml	35-40%	1.2
7	**Rum**	1 peg	30 ml	37-42%	1.2
8	**Vodka**	1 peg	30 ml	35-50%	1.2
9	**Liqueur**	1 peg	30 ml	15-30%	1
10	**Absinthe**	1 shot	30 ml	45-75%	2.1

➢ **DOSE**

1 Standard drink = 330 - 350 ml of beer, 140 -150 ml of wine, 40 - 45 ml of whisky/rum/vodka

- **Males:-** Normal dose ; upto 2 standard drinks per day and maximum 14 drinks per week
- **Females:-** Normal dose ; upto 1 standard drink per day and maximum 7 drinks per week

NOTE

✓ Daily drinking is not healthy even if the quantity is low.

✓ Special Populations such as Pregnant women and Adolescents [<18 years] was not suitable for drink alcohol.

➢ **MECHANISM OF ALCOHOL**[8][9][10]

Alcohol was believed to enhance CNS depression by a generalized membrane action alters the state of membrane consisting Lipids and also decrease the effect on multiple receptor operated and voltage gated ion channels and other critical proteins has been illustrated at concentrations attained during mild to moderate drinking. Thus several systems are affected especially Neural and hormonal systems are the same time affected producing by other depressants drugs such as **Barbiturates** and **Benzodiazepines** which predominantly facilitate GABAA receptor mediated Cl^- opening. Alcohol has been shown to increase **GABA** release at **$GABA_A$ sites** in the **brain**.

It also hinder **NMDA** and **kinate type of excitatory amino acid receptors**. Alcohols also acts on 5-HT3 inhibitory receptors is increased. On the other hand, the receptors named Cerebral Nicotinic Cholinergic Receptors which are opening via Na^+ channel.

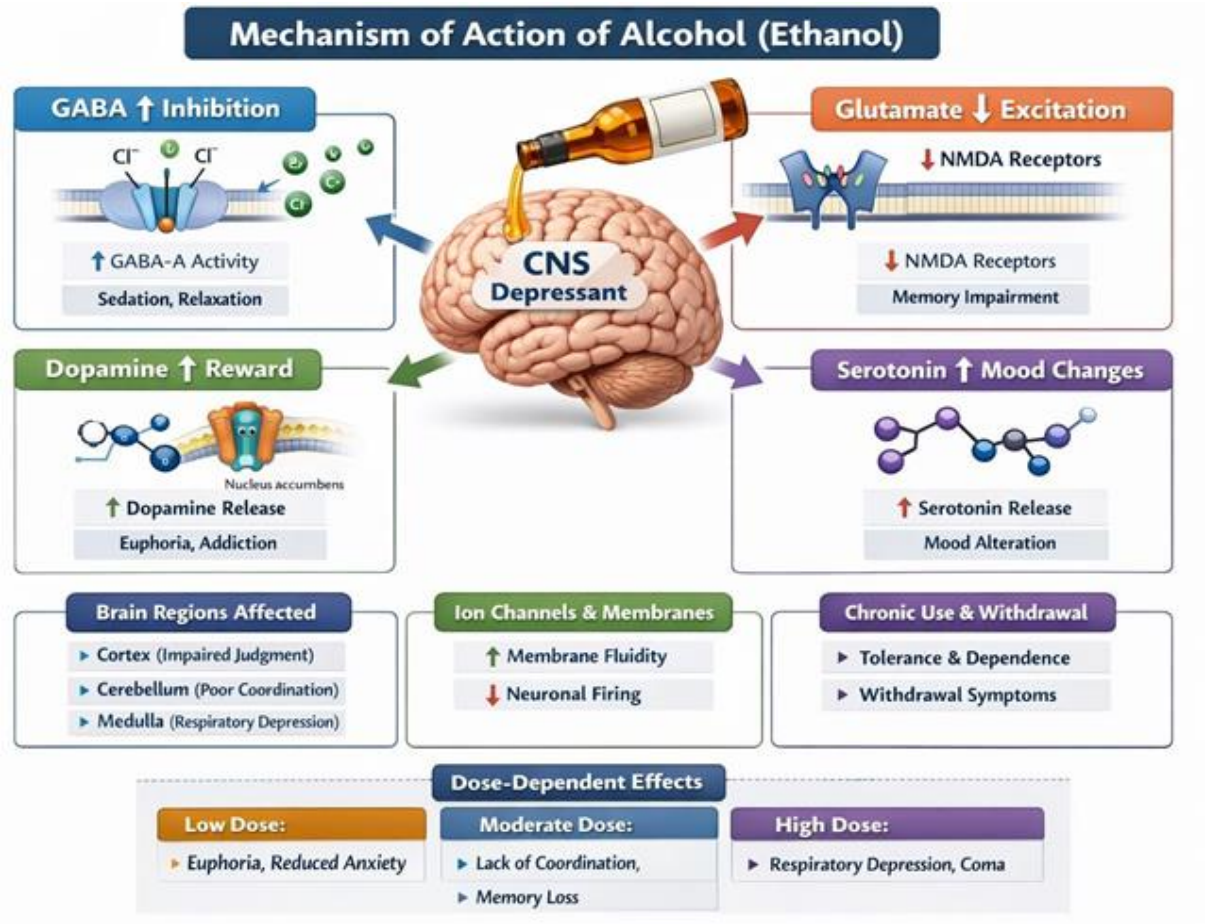

Figure No. 01: Mechanism of Alcohol.

➢ USES OF ALCOHOL[11]

Figure No. 02: Uses of Alcohol.

➢ CONTRAINDICATIONS[12,13,14,15,16,17]

- **In pregnancy**, Ethanol act as a teratogen - a substance that causes birth defects due to it can across cell membranes, the blood brain barrier, and the placenta of developing fetuses inducing oxidative stress, mitochondrial damage, and apoptosis/cell death.

- **Peptic ulcer disease,** alcohol its ability to irritate the stomach lining, enhance stomach acid (HCl) production, and decrease the healing process of existing ulcers.
- **Diabetics,** Alcohol can considerably lowers the blood sugar levels, principally when they drink with empty stomach or concurrence with diabetic medications.
- **Allergic Reactions,** Alcohol especially Regular Beer or any Wine contains high concentration of Histamine which can develop the allergy like reactions those are Runny nose, Headaches, Hives etc.
- And some other contraindications are **Liver diseases** such as Alcoholic hepatitis, Liver cirrhosis, Fatty liver disease etc ; **Acute or Chronic Pancreatitis**; **Cardiovascular issues** such as Hypertension, Cardiomyopathy, Arrhythmias.
- There are some of the medications which are directly interact with the alcohol such as, **Metronidazole, Disulfiram, Benzodiazepines, Antipsychotics, NSAIDs, Antidepressants, Anticonvulsants, Insulin** etc.

➢ ADVERSE DRUG REACTIONS[18,19,20,21,22,23,24,25]

- **Central Nervous System**

✓ Headaches, are common with alcohol intake. On long term usage cause damage to brain such as Stoke and Dementia.

✓ Alcohol can cause Nerve damage and result in numbness , pain in upper and lower limbs.

✓ Alcohol can also interfere with a numerous neurotransmitters in our body leads to lowering of several functions such as Brain activity, Energy levels.

- **Cardio Vascular System**

✓ Hypertension (increased BP), Cardiac Arrhythmias, Heart attack, Strokes, Heart burn.

- **Gastro Intestinal System**

✓ Mainly affect the salivary glands and decrease the saliva production can cause impairment in defense mechanisms against microorganisms.

✓ Heavy consumption of alcohol can cause damage to pancreas leads to Pancreatitis.

✓ Long term intake of alcohol can experience the Gastritis, Ulcers to stomach.

✓ On single drinking session Fatty liver, on heavy drink advanced Liver Disease was caused to Liver.

- **Skin**

✓ On initial stages Alcohol can cause dryness, redness to skin , overtime it may contribute to diseases such as Psoriasis, Skin infections.

- **Renal**

✓ Large amount of alcohol can increase the stress on Kidneys, sometimes can cause Back pain, on severe drink can cause Kidney diseases.

✓ Alcohol interferes with the kidney's ability to retain water, making bladder fill faster and promotes dehydration.

- **Musculoskeletal System**

✓ Long term alcohol misuse can cause weakens bones, making Osteoporosis and Fractures more likely.

- **Reproductive System**

✓ Ongoing alcohol use can reduce fertility for both sexes, whereas in females on long run may disrupt menstrual cycles.

- **Others**

✓ **Mental Health**; Alcohol can aggravate existing mental health issues and make emotional issues harder to manage.

✓ **Eyes,** Drinking may cause blurry or double vision along with redness from dilated blood vessels in the eyes.

✓ Intake of alcohol can affect all the systems in our body especially nervous system (Brain), GIT, Liver and Kidneys.

➢ ALCOHOL CAUSING DISEASES[95]

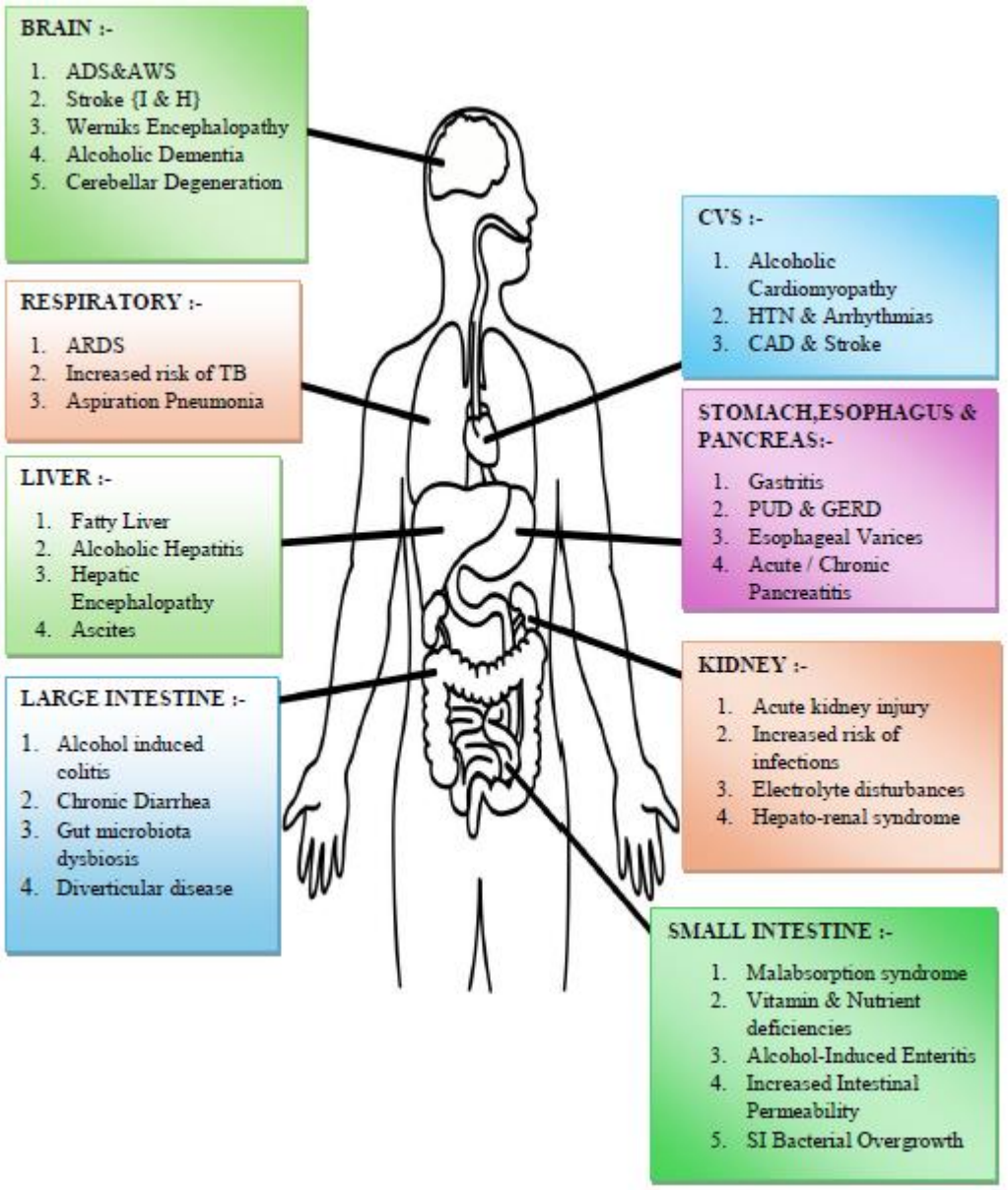

Figure No. 03 Alcohol causing diseases.

ALCOHOL DEPENDENCE SYNDROME (ADS)

➢ DEFINITION[26]

As per WHO [ICD 10] guidelines Alcohol Dependence Syndrome {ADS} is a group of physiological, behavioral and cognitive changes in which alcohol consumption becomes a dominant priority for an individual, overriding other activities and interests that were previously important. A core feature is a powerful craving or compulsion to consume alcohol. The diagnosis is established when three or more characteristic features occur together at any time within the preceeding 12 months.

➢ EPIDEMIOLOGY[27][28]

- **Global Prevalence**

✓ ADS affects approximately 2 -3 % of the Adult population in the world as per ICD 10 guidelines.

- **Gender Distribution**

✓ This disorder is significantly more prevalent in males than females, with the ratio of 3-5[Male] : 1 [Female].

- **Age Distribution**

✓ ADS commonly begins in late adolescence or early adulthood. Highly seen in 20-50 years of age groups.

- **Geographic variation**

✓ Higher prevalence in Europe and Americas.

✓ Moderately seen in South-East Asia

✓ Less seen in Eastern Mediterranean regions

- **India**

✓ In India Alcohol Dependence is estimated to affect 4-10% in adult males whereas prevalence among females remains low.

- **Socioeconomic Factors**

✓ More commonly seen in Individuals with unemployment, psychiatric co- morbidities and in lower socio- economic groups.

➢ WHEN TO SUSPECT ALCOHOL DEPENDENCE SYNDROME

❖ ADS is suspected when an individual presents with a **pattern of chronic& compulsive alcohol consumption** associated with behavioral, cognitive and physiological changes.

❖ Suspicion of ADS arises when a person reports **craving** for alcohol plus difficulty in controlling the onset, termination of drinking.

❖ Another clinical feature is the occurrence of withdrawal symptoms such as tremors anxiety nausea insomnia seizures or delirium upon cessation of alcohol intake.

❖ Another feature is despite having clear evidence of harm medical complications such as liver disease, gastritis, pancreatitis, psychological problems alcohol use continues.

- An important indicator is the **TOLERANCE**. Tolerance is indicated by the need for progressively increasing amounts of alcohol to achieve the same intoxicating effect.
- Repeated unsuccessful attempts to cut down drinking strengthen the suspicion of dependence.
- Early identification is necessary as timely intervention can reduce morbidity, prevent complications and improve long term outcomes.

➢ ETIOLOGY[29,30,31,54]

1. Biological Factors

a. Genetic Predisposition

b. Neurotransmitter imbalance, Imbalance between Dopamine, GABA and Glutamate neurotransmitters. Decreased GABA and Increased Glutamate causes tolerance and withdrawal symptoms.

c. Metabolic Factors

Variations in the Alcohol metabolizing enzymes [ADH & ALDH]

2. Psychological Factors

a. Personality Traits ; Low self esteem, impulsivity

b. Stress coping; Alcohol is used to relieve Anxiety, Depression

c. Psychiatric Comorbidities such as Depression, PTSD, Anxiety Disorders

3. Early Age of Initiation

a. Early exposure of alcohol interferes with the development of brain and increases the risk of dependence

4. Social and Environmental Factors

a. Family Environment

b. Parental drinking, Poor supervision

➢ PATHOPHYSIOLOGY[32,33,34,62]

Chronic intake of Alcohol produces changes in brain neurotransmitters. Alcohol increases the **GABA neurotransmitter** and decreases the **Glutamate neurotransmitter** causing relaxation and sedation. It also increases the Dopamine levels in the brain reward pathway which produce pleasure and inspire to take alcohol. With repeated alcohol consumption the

brain slowly adapts to these effects. As a result tolerance develops and more amount of alcohol is needed to achieve the same effect which ultimately causes to physical and psychological dependence on alcohol. When alcohol intake is suddenly stopped GABA activity decreases and Glutamate increases which leads to increased Brain Excitability and the individual develops withdrawal symptoms such as Tremors, Anxiety, Seizures. This neuroadaptive changes together results in **ALCOHOL DEPENDENCE SYNDROME.**

Figure No. 04: Pathophysiology of Alcohol Dependence Syndrome.

➢ RISK FACTORS [35]

1. Male sex 5. Occupational Factors

2. Chronic Medical illness 6. Early age of alcohol use
3. Lack of social support 7. Personality traits
4. Comorbid psychiatric disorders 8. Peer Pressure

- **SIGN AND SYMPTOMS**[37,38]

NOTE:- Lifetime risk for Alcohol use for men is 10-15% and for women is 5-8%

1. **Psychological Manifestations**

a. Strong cravings
b. Anxiety , Restlessness
c. Sleep disturbances
d. Cognitive impairment
e. Mood swings

2. Behavioral Manifestations

a. Drinking early in the morning (eye opener)
b. Hard to stop alcohol intake
c. Loss of control on overdrinking
d. Neglect on their own responsibilities

3. **Withdrawal Symptoms**

a. Nausea and Vomiting
b. Sweating
c. Palpitations
d. Seizures
e. Tremors

4. **System wise Manifestations**

a. Neurologic symptoms :- Seizures,

Delirium Tremens, Cerebellar degeneration

b. GIT :- Esophagitis, Gastritis, Pancreatitis, Hepatitis
c. CVS :- Hypertension, Cardiomyopathy
d. Hematologic :- Macrocytosis, Thrombocytopenia, Leucopenia, Folate deficiency
e. Endocrine :-Gynecomastia, Testicular Atrophy, Amenorrhea, infertility
f. Cancer: breast cancer, oral &esophageal cancer, rectal cancers.

➢ DIAGNOSIS[39,40]

The NICE Public Health Guidelines on reducing harmful drinking recommends a session of brief structured advice based on **FRAMES principles** (F= Feedback, R= Responsibility, A= Advice, M=Menu, E=Empathy, S=Self efficacy) has a useful intervention for everyone obtain the risk of alcohol related problems.

➢ **Where consumption above recommended levels has been identified a more details of clinical assessment is required they include as follows**

a. H/o Alcohol use , including daily consumption and recent pattern of drinking
b. H/o Previous episodes of alcohol withdrawal
c. Time of last recent drink
d. H/o from Family members OR carrier
e. Other drugs (Illicit and prescribed) usage
f. Severity of dependence and withdrawal symptoms
g. Co-exciting medical and psychiatric risks
h. Physical examination, including cognitive function

✓ **Laboratory investigations**

i. Full Blood count [FBC]
ii. Urea and electrolytes [U&E]
iii. Liver Function Tests[LFTs],
iv. Prothrombin Time [PT]
v. Urinary drug screen

✓ **Scales used**

SADQ (Severity of Alcohol Dependence Questionnaire)

Table No. 02 SADQ scale score.

SL.NO	SCORE	SEVERITY
1	16	Mild
2	16 – 30	Moderate
3	30 or more than 30	Severe

➢ COMPLICATIONS[41,42,43]

1. Alcoholic Fatty Liver
2. Peripheral Neuropathy
3. Alcoholic Hepatitis
4. Wernike's Encephalopathy
5. Alcohol Withdrawal Syndrome
6. Korsakoff Syndrome
7. Sleep abnormalities
8. Liver Cirrhosis

- **MANAGEMENT**
- **Non Pharmacological Treatment**[44,45,46,47,52,54,55]

The main aim is to achieve abstinence, prevent relapse and improve the psychological functioning.

a. Motivational Interviewing

- Resolves ambivianence
- Increase readiness to quite

b. Cognitive Behavior Therapy – identify the triggers such as stress, emotions and modify maladaptive thoughts.

c. Relapse prevention therapy – identify the high-risk situations and trains the patients to manage cravings and lapses. Reduces risk of full relapse after abstinence.

d. Supportive psychotherapy–provides emotion support and reassurance. Improves self-esteem and coping ability. Enhances adherence to long term treatment.

e. Lifestyle modification

- Encourages structured daily routine and health habits
- Improves physical and mental well being
- Reduces stress related relapse risk

- **Pharmacological Treatment**[48,49,51,89,96,97]

Table No. 03: Pharmacological Treatment of ADS.

SL.NO		DRUG	DOSE	ROA	FREQUENCY	DURATION
I	**BENZODIAZEPINES**					
	1	**Diazepam** (Long acting)	10 – 20 mg	Oral/IV	Every 1 -2 hours	Mild : 3 – 5 days Moderate : 5 -7 days Severe : 7 – 10 days
	2	**Chlordiazepoxide** (Long acting)	25 – 100 mg	Oral	Every 4 – 6 hours	
	3	**Lorazepam** (Short acting)	2 – 4 mg	Oral/IV/IM	Every 4 – 6 hours	3 – 7 days
	4	**Oxazepam** (Short acting)	15 – 30 mg	Oral	Every 6 – 8 hours	
II	**AVERSION THERAPY**					
	1	**Disulfiram**	250 – 500 mg	Oral	OD	6 months to 1 year
III	**ANTI – CONVULSANTS**					
	1	**Carbamazepine**	200 mg	Oral	BD/TID	5 – 7 days
	2	**Sodium Valproate**	250 – 500 mg	Oral	BD/TID	
IV	**VITAMIN SUPPLEMENTS**					
	1	**Thiamine**	100 mg	IV/IM -	OD/BD	3-5 days IV then

				Oral		Oral for weeks
V	**ANTI – PSYCHOTICS (ADJUNCT)**					
	1	**Haloperidol**	2 -5 mg	Oral/IM	BD	3 – 5 days
VI	**OPIOID ANTAGONISTS**					
	1	**Naltrexone**	50 mg	Oral	OD	3 months
	2	**Naltrexone (Depot)**	380 mg	IM	Once Monthly	6 – 12 months
VII	**GLUTAMATE MODULATOR**					
	1	**Acamprosate**	666 mg	Oral	OD	6 – 12 months
VIII	**ALPHA – 2 – ADRENERGIC AGENTS**					
	1	**Clonidine**	0.1 – 0.2 mg	Oral	BD	3 – 5 days
IX	**BETA BLOCKERS**					
	1	**Propranolol**	20 – 40 mg	Oral	BD	3 – 5 days
X	**GABA – B AGONIST**					
	1	**Baclofen**	5 – 10 mg up to 30 – 60mg	Oral	BD	3 – 12 months

ALCOHOL WITHDRAWAL SYNDROME (AWS)

➢ DEFINITION[56]

Alcohol withdrawal syndrome is a group of symptoms of varying severity that occur on absolute or relative withdrawal of alcohol after persistent, excessive and prolonged use. It is characterized by the development of autonomic hyperactivity, tremors, insomnia, hallucinations etc, AWS is seen in chronic, dependent drinkers due to neurotransmitter imbalance (GABA, Glutamate).it ranges mild tremors to delirium tremens.

➢ EPIDEMIOLOGY[59]

- **Prevalence**

✓ Mostly 50 to 60% of cases is seen in chronic alcoholic patients

✓ Severe AWS (seizures and delirium) is seen in 5 to 10% of cases

- **Age Distribution**

✓ Mostly seen in middle age adults (30 to 60)

✓ Severity increases with age

- **Gender Distribution**

✓ More common in males, females may develop AWS with lower quantities because of physiological differences.

- **Socioeconomic Factors**

✓ Higher prevalence seen in urban populations, individuals have in low income status.

- **ETIOLOGY**[29,30,31,54,57]

1. Abrupt cessation of alcohol

a. This is the most common and direct cause seen in a person who consumes alcohol for a long time and develop adaptation which causes withdrawal symptoms when he suddenly stopped drinking alcohol.

2. Reduction in alcohol intake

a. Significant reduction alcohol intake can trigger withdrawal symptoms

b. This is commonly occurs during the hospitalization, illness

3. Neurochemical imbalance

a. Imbalance between inhibitory GABA neurotransmitter and excitatory glutamate neurotransmitter causes CNS excitability and produce withdrawal symptoms

4. Electrolyte Disturbances & Liver impairment

a. Alcohol use is associated with electrolyte imbalances like potassium and sodium which increases neuronal excitability and causes seizures during withdrawal. Liver disease impairs the metabolism of alcohol and neurotransmitters producing toxic substance accumulation and their by increasing the severity of withdrawal symptoms.

➢ PATHOPHYSIOLOGY[32,33,34,58,59,60,61]

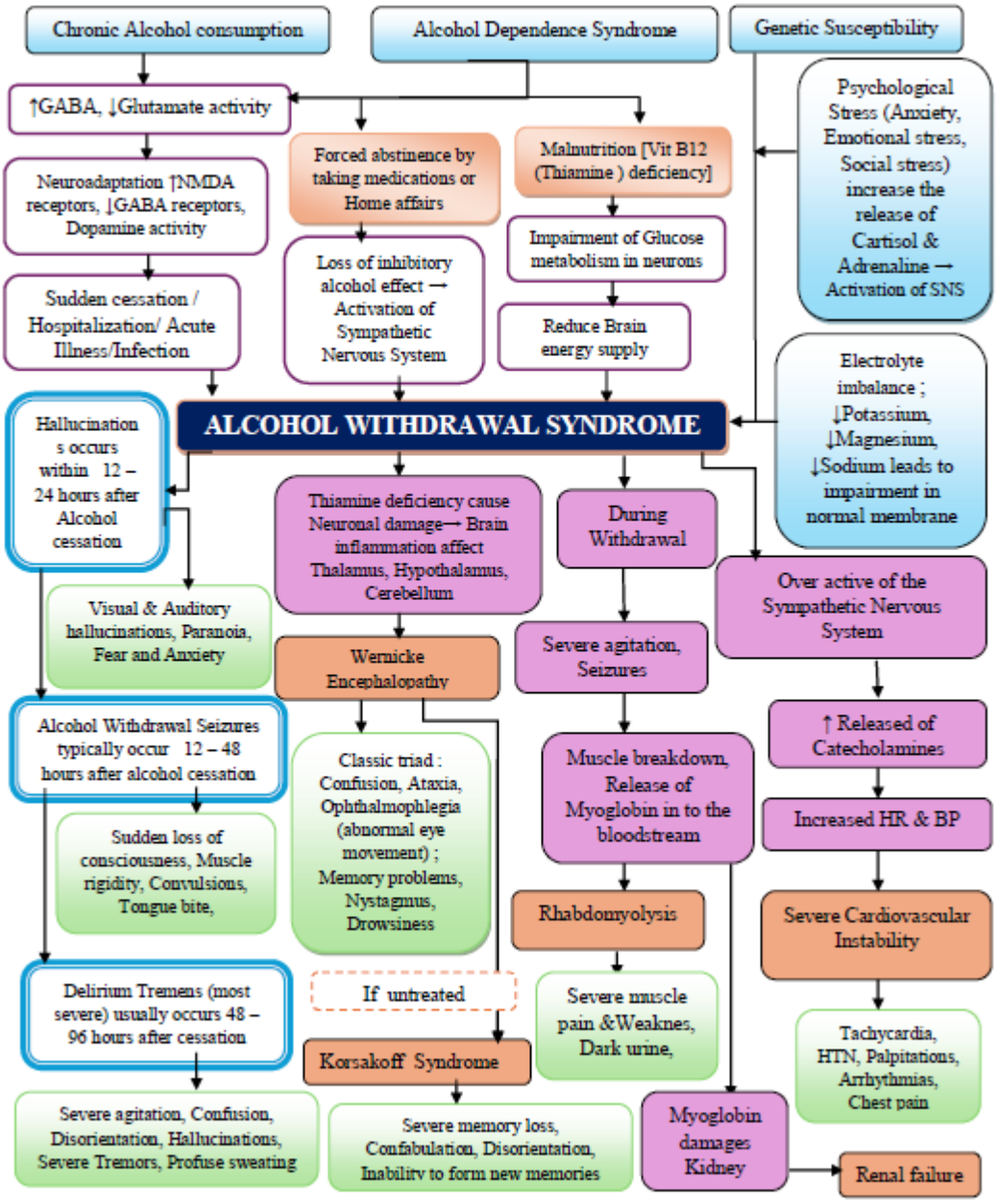

Figure No. 05: Pathophysiolgy of Alcohol Withdrawal Syndrome.

On Chronic alcohol intake decrease autonomic Adrenergic systems and decrease the Dopamine levels in the Nucleus accumbens [increase Alcohol depressant levels on brain] enhance the depressant effects on brain. This may cause decrease Glutamte induced excitation and increase GABA induced inhibition progress Long term Physical dependence.

On sudden cessation of Alcohol can observe decreased levels of EtOH{Alcohol} in blood which contributes to Alcohol Withdrawal Syndrome. The core mechanism involved is as follows

i. AWS increase Autonomic adrenergic system enhances the Sympathetic effects such as increased Heart rate, Respiratory rate, Blood pressure and diaphoresis.

ii. On the other hand in AWS decreased GABA induced inhibition and inAlcohol Withdrawal Syndrome occurs when a person with chronic and heavy alcohol use suddenly reduces or stops alcohol.

➢ SIGNS & SYMPTOMS[58,59,60,61]

1. The **early stage** symptoms that arise during 6-12 hours of alcohol cessation are Insomnia, Tremors, Anxiety, Digestive upset, Headache, Sweating, Palpitations.
2. In **intermediate stage** i.e. 12-24 hours visual, auditory and tactile hallucinations can be seen along with increased tremors, agitation.
3. In the seizure stage i.e. 24 – 48 hours generalized tonic- clonic seizures can be observed .
4. The most severe form is **Delirium Tremens** which occurs after 48 hours which is characterized by severe confusion, disorientation, consciousness fluctuations, vivid hallucinations, agitation and autonomic instability [hyperthermia, tachycardia, hypertension], tremors.

➢ DIAGNOSIS[62,63]

- AWS is primarily a clinical diagnosis based on0

a. History

b. Typical symptoms

- Diagnostic criteria [DSM – 5]

a. Cessation or reduction in heavy and prolonged alcohol use

b. Within hours to days, ≥ 2 of the following

Those are Autonomic hyperactivity {Sweating, Tachycardia}, Hand tremors, Insomnia, Nausea or Vomiting, Transient Hallucinations {Visual , Auditory, Tactile}, Psychomotor agitation , Anxiety, Generalized tonic clonic seizures.

Note:- Symptoms not due to another medical condition.

✓ Laboratory test (supportive , not confirmatory)

i) CBC (Complete Blood Count)

ii) Sr electrolytes

iii) LFT

iv) Blood glucose levels

✓ **Scale Used**[63]

CIWA–Ar SCALE [Clinical Institute Withdrawal Assessment for Alcohol (Revised)] (Severity Assessment)

Table No. 04: C1WA – Ar Scale score.

SL. NO	SCORE	SEVERITY
1	<8	Mild
2	8 – 15	Moderate
3	>15	Severe { Risk of DT and Seizures }

➢ **COMPLICATIONS**[41,42,43,44,45]

1. Wernike Encephalopathy
2. Korsakoff Syndrome
3. Renal failure
4. Severe Cardiovascular Instability
5. Rhabdomyolysis

➢ **MANAGEMENT**

- **Non pharmacological treatment**[64,65]

1. Supportive care

a. Quite, calm environment produces agitation, anxiety, hallucinations

b. Minimal stimulation

2. Hydration and Nutrition :-

a. Adequate fluid intake prevents dehydration

b. Maintain balance diet with high proteins and calories and correct electrolyte (sodium Na^+, potassium K^+, Magnesium Mg^{2+})

3. Vitamin supplementation

Majorly vitamins are given as injections or tablets. Vitamin B1 (Thiamine) prevents Wernicke's encephalopathy, Korsakoff syndrome

Note:- Thiamine is given before Glucose administration

4. Regular Monitoring and Observation

a. Pulse rate, Blood Pressure, Temperature, Respiratory rate are monitored regularly.

b. CIWA – Ar Score monitoring is required to assess the severity .

5. Maintain Sleep Hygiene :-

a. Maintain normal sleep wake cycle

b. Avoid unnecessary disturbances during night times

c. Avoid day time naps.

- **Pharmacological Treatment**[64][65][89][96][97]

Table No. 05: Pharmacological Treatment of AWS.

SL.NO		DRUG	DOSE	ROA	FREQUENCY	DURATION
I	**BENZODIAZEPINES**					
	1	**Chlordiazepoxide**	Mild: 25-50 mg Moderate to Severe: 50 – 100 mg	Oral	BD	3 – 7 days
	2	**Diazepam**	Mild: 5 – 10 mg Moderate: 10 – 20 mg Severe: 20 mg	Oral/ IV	BD	3 – 7 days
	3	**Lorazepam**	2 – 4 mg Severe : 4 mg	Oral/ IV	BD	3 – 7 days
II	**VITAMIN SUPPLEMENTS**					
	1	**Thiamine**	Mild: 100 mg Moderate: 100 - 200mg Severe: 200 – 500 mg	Oral/ IM	OD/ TDS	5 – 7 days
III	**BETA – BLOCKERS**					
	1	**Propranolol**	20 – 40 mg	Oral	BD	3 – 5 days
IV	**ALPHA – 2 – ADRENERGIC AGENTS**					
	1	**Clonidine**	0.1 mg	Oral	QID	>3 days
V	**ELECTROLYTE SUPPLEMENTATION**					
	1	**Magnesium Sulphate**	1 – 2 g	IV	OD/BD	Based on levels
VI	**ANTI – PSYCHOTICS**					
	1	**Haloperidol**	2 – 5 mg	IM/IV	BD – PRN	Short term
VII	**BARBITURATES**					
	1	**Phenobarbitol**	60 – 120 mg	IV	Every 20 – 30 min	PRN
VIII	**SEDATIVES**					
	1	**Propofol**	As needed	IV Infusion	BD	3 – 5 days

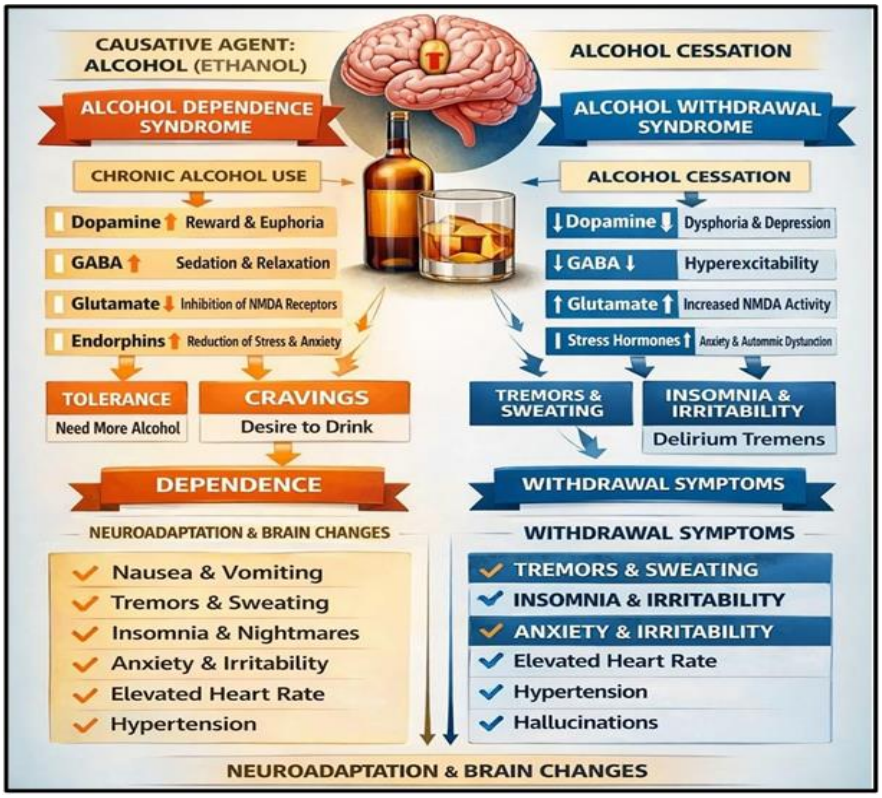

Figure No. 06: Comparison of ADS & AWS.

SLEEP ABNORMALITY

Sleep and cognitive impairment have a strong bidirectional link, where poor sleep (too little, too much, disrupted) impairs functions like focusing, attention, memory, language, visual and spatial processing etc.

Sleep disturbance is the main and persistent feature in Alcohol withdrawal and Dependence syndrome. It results from neuro chemical imbalance, circadian rhythm disruption and altered sleep architecture.[66,67,99]

➢ NORMAL SLEEP PATTERN[68,69,70,99]

Sleep is a normal regular daily pattern usually at night. It is a natural condition that happens everyday. During sleep, a person is not fully conscious but they are not unconscious either. They can still woke up by strong sounds, light, or touch, which is why sleep is reversible state and also while sleeping awareness of surroundings is reduced.

The sleep pattern is regularly controlled by body's internal clock , known as **Circadian Rhythm,** which tells us when to feel sleepy and when to feel alert. Sleep is also controlled by sleep pressure **[Homeostatic sleep drive]**.The longer we stay awake, the stronger the need for

sleep becomes, after sleep this pressure reduces, helping us feel refreshed.

Sleep Architecture

Sleep consists of **three** major types

a. Stage W
b. NREM Sleep [75 – 80 %]
c. REM Sleep [20 – 25 %]

a. Stage W [Wake Stage]

This is the initial stage of sleep mainly depends on whether eyes are open or closed, characterized by a person is conscious, alert and responsive to the environment.

b. NREM Sleep [Non Rapid Eye Movement Sleep]

- **Stage 1 (Light Sleep) {N 1}:-** 2 – 5 % of total sleep, it is a transition from wakefulness to sleep has slow eye movements and easily arousal.
- **Stage 2 (True Sleep) {N 2}:-** 45 – 55 % of total sleep, characterized by decreased Heart rate and body temperature and memory consolidation begins.
- **Stage 3 (Slow Wave / Deep Sleep) {N 3} :-** 15 – 25 % of total sleep, in this stage the brain and body are in their lowest level of activity making awaking difficult.

c. REM Sleep [Rapid Eye Movement] (Dream Sleep)

20 – 25 % of total sleep, is a distinct stage of sleep characterized by rapid eye movements, vivid dreaming and high brain activity. It is also called **Paradoxical sleep** because the brain appears awake while the body is asleep.

Figure No. 07: Various stages of Sleep cycle.

SLEEP DISTURBANCES IN ALCOHOL DEPENDENCE SYNDROME

Sleep disturbances are highly prevalent in individuals with alcohol dependence, although alcohol may initially induce sleep, chronic alcohol use causes persistent disruption of sleep architecture which results in poor sleep quality and day time dysfunction.

In chronic alcohol dependence sleep disturbance occur because of neurotransmitter imbalance, suppression of REM sleep and Circadian rhythm dysfunction. These changes continues even during abstinence and can increase the risk of relapse.[70,99]

SLEEP DISTURBANCES IN ALCOHOL WITHDRAWAL SYNDROME

Most common and persistent symptom of alcohol withdrawal is the sleep disturbance. Chronic alcohol use normally alters sleep architecture and when alcohol intake is suddenly stopped the central nervous system becomes hyper- excitable resulting in significant sleep problems. These disturbances begin within hours of cessation and may persist for weeks to months and can increase the risk of relapse. [71]

- **MECHANISM**[72,73,99]

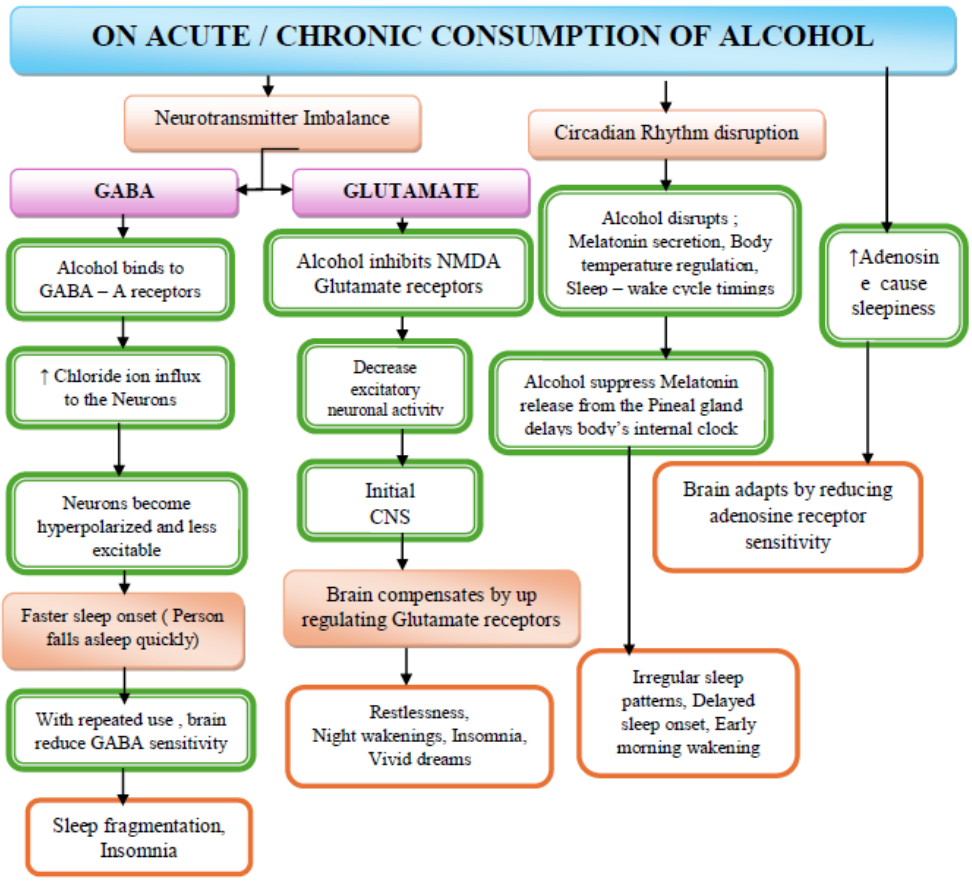

Figure No. 08: Mechanism of Alcohol induced Sleep abnormality.

➢ SIGNS & SYMPTOMS[73,74,75]

i. Restlessness
ii. Nightmares
iii. Frequent awakenings
iv. Irregular sleep patterns
v. Delayed sleep patterns
vi. Reduced natural sleep drive
vii. Chronic insomnia
viii. Night awakenings
ix. Palpitations
x. Oxygen desaturation

Feature	Acute Alcohol Effect	Chronic Alcohol Effect
Sleep onset	Faster sleep	Difficulty sleeping
REM sleep	Suppressed early	Rebound and abnormal REM
Sleep quality	Fragmented later night	Persistent insomnia
Daytime effect	Temporary drowsiness	Chronic fatigue and cognitive impairment

Differences of Signs and Symptoms of Sleep abnormality in Acute & Chronic alcohol intake

➢ DIAGNOSIS[75]

- Sleep history
- Medical and psychiatric history
- DSM – 5 Diagnostic crieteria
- Sleep assessment scale

Pittsburgh Sleep Quality Index Sclale (PSQI)

Table No. 07: PSQI scale score.

SL. NO	SCORE	SEVERITY
1	0 – 4	Normal
2	5 – 9	Mild
3	10 – 14	Moderate
4	14 – 18	Severe

➢ COMPLICATIONS[41][42]

1. Cognitive impairment
2. Daytime fatigue
3. Psychiatric diseases (Depression, Anxiety diseases, Mood instability)
4. Increased risk of relapse
5. Delirium Tremens

➢ MANAGEMENT

- **Non – Pharmacological Treatment**[76][77]

1. **Sleep hygiene education**

a. Maintain regular sleep and wake up time

b. Avoid Caffeine, Nicotine &Alcohol before bedtime

c. Avoid heavy meals before sleep

d. Encourage day time physical activity

2. Cognitive Behavioral Therapy for Insomnia

a. Stimulus control therapy

b. Relaxation therapy

c. Stress restriction therapy

d. Cognitive therapy

3. Lifestyle Therapy :-

a. Stress management

b. Yoga and Meditation

c. Avoid daytime naps

- **Pharmacological Treatment**[78,79,80,89,96]

Table No. 08: Pharmacological Treatment of Sleep Abnormality.

SL. No		DRUG	DOSE	ROA	FREQUENCY	DURATION
I	BENZODIAZEPINES					
	1	**Diazepam**	5 – 10 mg	Oral /IV	OD to TID (depend on severity)	3 – 7 days
	2	**Lorazepam**	1 – 2 mg	Oral / IV	BD/TID	3 – 5 days
	3	**Chlordiazepoxide**	25 – 50 mg	Oral	BD/ TID	5 – 7 days
II	NON – BENZODIAZEPINE HYPNOTICS					
	1	**Zolidem**	5 – 10 mg	Oral	HS	2 – 4 weeks
	2	**Zoleplon**				
III	SEDATIVES					
	1	**Trazodone**	50 – 100 mg	Oral	HS	2 – 6 weeks
	2	**Mirtazepine**	7.5 – 10 mg	Oral	HS	2 – 6 weeks
IV	MELATONIN – RECEPTOR AGONIST					
	1	**Melatonin**	3 – 5 mg	Oral	HS	2 – 4 weeks
V	ANTI – CRAVING AGNET					
	1	**Acamprusate**	666 mg	Oral	BD	3 – 6 months
	2	**Naltrexone**	50 mg	Oral	OD	3 – 6 months
VI	ALCOHOL DETTERENT					
	1	**Disulfiram**	50 – 200 mg	Oral	OD	Long term
VII	VITAMIN SUPPLEMENTS					
	1	**Thiamine**	100 mg	Oral /IM	OD	1 – 2 weeks

➢ COMPARISION OF SLEEP ABNORMALITY IN ADS & AWS

Table No. 09:Comparison of Sleep abnormality in ADS & AWS.

Parameter	Alcohol Dependence Syndrome (ADS)	Alcohol Withdrawal Syndrome (AWS)
Definition	Chronic sleep disturbances caused by prolonged alcohol consumption affecting sleep regulation.	Acute sleep disturbance occurring after sudden reduction or cessation of alcohol in dependent individuals.
Onset	Gradual development with long- term alcohol use.	Begins within **6–48 hours** after stopping alcohol.
Sleep Latency	Initially decreased (faster sleep onset), but later **increased difficulty in falling asleep**.	Markedly increased; severe **insomnia** is common.
Total Sleep Time	Reduced due to fragmented and poor-quality sleep.	Significantly decreased because of agitation and withdrawal symptoms.
Sleep Quality	Poor sleep quality with frequent awakenings.	Very poor sleep with restlessness and inability to maintain sleep.
REM Sleep	**Suppressed REM sleep** during alcohol use; REM rebound occurs during abstinence.	**Marked REM rebound**, leading to vivid dreams and nightmares.
Slow Wave Sleep (Deep Sleep)	Decreased slow wave sleep over time.	Highly disturbed or reduced deep sleep.
Sleep Fragmentation	Frequent nighttime awakenings.	Severe fragmentation due to autonomic hyperactivity and anxiety.
Nightmares / Vivid Dreams	May occur occasionally in chronic users.	Very common due to REM rebound.
Daytime Sleepiness	Excessive daytime sleepiness and fatigue.	Fatigue due to **severe insomnia** during withdrawal.
Circadian Rhythm	Disrupted circadian rhythm with irregular sleep patterns.	Temporary circadian disturbance due to withdrawal stress.
Severity	Chronic and persistent if alcohol use continues.	Acute but intense during withdrawal phase.
Duration	May persist for weeks or months even after abstinence.	Usually improves within **3–7 days** with treatment.
Reversibility	Partially reversible with prolonged abstinence and sleep therapy.	Mostly reversible with appropriate withdrawal management (e.g., benzodiazepines).

COGNITIVE IMPAIRMENT

Cognitive impairment is a disturbance or decline in one or more cognitive domains such as attention, memory, learning, language, executive function, visuospatial abilities, or social cognition, which represents a change from a previous level of functioning and may interfere to a variable degree with daily activities.[81]

TYPES[82,123]

A. Based on Severity

1. Mild Cognitive Impairment [MCI]

- ✓ Mild problems with memory or thinking
- ✓ Person can still do daily activities independently
- ✓ May or may not progress to dementia
- ✓ Example: forgetting appointments but remembering later

2. Major cognitive impairment [Dementia]

- ✓ Severe and progressive loss of thinking abilities
- ✓ Affects daily life and independence
- ✓ Includes memory loss, confusion, personality changes

B. Based on affected cognitive domain

1. Memory impairment:

- ✓ Difficulty remembering recent events
- ✓ Seen in alzheimers disease, amnesia

2. Attention impairment

- ✓ Difficulty concentrating or sustaining focus
- ✓ Common in ADHD, delirium, depression

3. Language impairment [aphasia]

- ✓ Problems with speaking, understanding, reading, or writing
- ✓ Often due to stroke or brain injury

4. Executive function impairment

- ✓ Poor planning, decision making, problem solving
- ✓ Seen in frontal lobe disorders

5. Visuospatial impairment

- ✓ Difficulty recognizing objects, faces, or navigating spaces
- ✓ Seen in dementia with lewy bodies, alzheimer's disease

C. Based on etiology

1. Neurodegenerative disorders

- ✓ Alzheimers disease
- ✓ Parkinson's disease dementia
- ✓ Frontotemporal dementia
- ✓ Lewy body dementia

2. Vascular cognitive impairment

- ✓ Due to reduced blood flow to the brain
- ✓ Often after stroke or chronic hypertension

3. Traumatic brain injury [TBI]

- ✓ Cognitive deficits following head injury

4. Metabolic and endocrine causes

- ✓ Hypothyroidism
- ✓ Vitamin B12 deficiency
- ✓ Hypoglycemia

5. Psychiatric causes

- ✓ Depression [pseudodementia]
- ✓ Schizophrenia

COGNITIVE IMPAIRMRNT IN ALCOHOL DEPENDENCE SYNDROME

Alcohol dependence syndrome is a chronic relapsing disorder characterized by compulsive alcohol use, tolerance, and withdrawal. Long term alcohol consumption leads to structural and functional brain changes, resulting in cognitive impairment. Textbooks describe this impairment as dose dependent, duration dependent, and partially reversible in early stages.

Cognitive impairment in alcohol dependence syndrome refers to decline in mental processes such as thinking, memory, reasoning and decision making caused by acute or prolonged usage of alcohol.[82]

COGNITIVE IMPAIRMRNT IN ALCOHOL WITHDRAWAL SYNDROME

Cognitive impairment in Alcohol Withdrawal Syndrome refers to temporary or persistent disturbances in mental functions such as memory, attention, orientation and decision making

that occurs during withdrawal period after cessation of alcohol.

It may caused due to Neurotransmitter imbalance such as ↑ Glutamate ↓ GABA, Thiamine deficiency, CNS Hyper excitability, Autonomic hyperactivity.[82]

- **SIGNS AND SYMPTOMS[82]**

i. Poor concentration
ii. Memory loss
iii. Confusion
iv. Poor judgment
v. Reduced attention span
vi. Severe confusion (in DT)
vii. Hallucinations
viii. Disorientation
ix. Agitation
x. Restlessness

- **MECHANISM[83]**

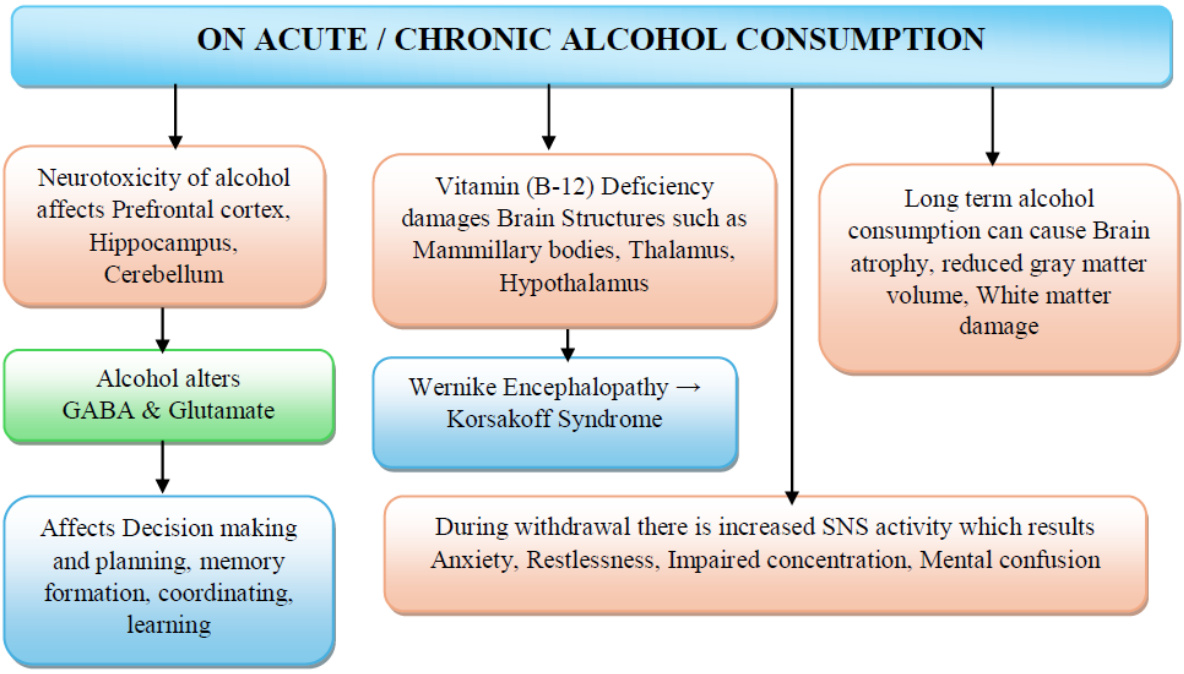

Figure No. 09: Mechanism of Alcohol induced Cognitive Impairment.

- **DIAGNOSIS[84]**

- Clinical assessment
- Scales used

Mini Mental Scale Examination (MMSC)

Table No. 10: MMSC Scale score.

SL. NO	SCORE	SEVERITY
1	24 – 30	Normal
2	18 – 23	Mild to Moderate
3	0 – 17	Severe

- **Laboratory examinations**

i. CBC

ii. Liver Function Tests

iii. Blood Glucose and Vitamin levels

- Neurological imaging by CT(Computerized Tomogarphy) SCAN, MRI (Magnetic Resonance Imaging)
- Neurological examination

➢ **COMPLICATIONS**[85]

1. Profound memory loss
2. Dementia
3. Alcohol related Brain changes
4. Wernike – Korsakoff syndrome

➢ **MANAGEMENT**[87]

- **Non pharmacological management**

1. Psychological interventions

a. Motivational interviewing

✓ Enhance motivation to quit

✓ Resolves ambivalence

b. **Cognitive behavior therapy**

✓ Identifies triggers & Prevents relapse

✓ Develops coping strategies

c. **Relapse prevention therapy**

✓ Managing high risk situations

✓ Craving control & Life style Modification

d. **Family therapy and social interventions**

- **Pharmacological management**[88,96,97]

Table No. 11: Pharmacological Treatment of Cognitive impairment.

SL. No		DRUG	DOSE	ROA	FREQUENCY	DURATION
I		**BENZODIAZEPINES**				
	1	**Lorazepam**	1 – 2 mg	Oral / IV	BD/TID	3 – 5 days
	2	**Chlordiazepoxide**	25 – 50 mg	Oral	BD/ TID	5 – 7 days
II		**VITAMIN SUPPLEMENTATION**				
	1	**Thiamine**	100 –200 mg	Oral/I V/IM	OD	1 – 2 weeks initially then maintainence
	2	**Folic Acid**	1 – 5 mg	Oral	OD	2 – 4 weeks
	3	**Vitamin – B Complex**	1 Tab	Oral	OD	
III		**ANTI – CRAVING AGENT**				
	1	**Acamprosate**	666 mg	Oral	BD/TID	3 – 6 months
IV		**ALCOHOL DETERRENT**				
	1	**Disulfiram**	250 mg	Oral	OD	Long term
V		**COGNITIVE ENHANCER**				
	1	**Donepezil**	5 – 10 mg	Oral	OD	1 – 2 months
VI		**NMDA RECEPTOR ANTAGONIST**				
	1	**Memantine**	5 – 20 mg	Oral	OD	1 – 2 months

➢ **COMPARISION OF COGNITVE IMPAIRMENT IN ADS & AWS**

Table No. 12: Comparison of Cognitive Impairment in ADS & AWS.

Parameter	**Alcohol Dependence Syndrome (ADS)**	**Alcohol Withdrawal Syndrome (AWS)**
Definition	Chronic cognitive impairment due to long-term excessive alcohol consumption causing neuroadaptation and brain damage.	Acute cognitive disturbances that occur after sudden reduction or cessation of alcohol in dependent individuals.
Onset	Gradual onset with prolonged alcohol use over months or years.	Sudden onset within **6–48 hours** after stopping or reducing alcohol intake.
Main Cause	Neurotoxicity of alcohol, thiamine deficiency, and structural brain damage.	Hyperexcitability of the CNS due to imbalance between **GABA inhibition and glutamate excitation**.
Attention & Concentration	Persistent difficulty in attention and reduced concentration.	Marked impairment in attention with fluctuating alertness.
Memory	Long-term memory deficits, especially **recent memory impairment**; may lead to **Wernick –Korsakoff syndrome**.	Temporary memory disturbances and confusion during withdrawal.
Orientation	Usually preserved in mild cases but may decline in severe chronic alcoholism.	Often **disoriented to time, place, and person**, especially in delirium tremens.
Learning Ability	Decreased learning capacity and difficulty acquiring new information.	Temporary difficulty processing new information due to agitation and

		confusion.
Reversibility	Partially reversible with prolonged abstinence, nutrition, and therapy.	Usually completely reversible with appropriate treatment (e.g., benzodiazepines).
Severity	Chronic and progressive if alcohol use continues.	Acute and reversible once withdrawal is treated.
Duration	Long-term impairment; may persist even after abstinence in severe cases.	Short-term; typically lasts **3–7 days** depending on severity.

DRUG INFORMATION ON LORAZEPAM & CHLORDIAZEPOXIDE

The drugs **Lorazepam** and **Chlordiazepoxide** belong to the category **Benzodiazepines**. These are psychoactive drugs widely used in the management of anxiety disorders, Alcohol syndromes (Withdrawal, Dependence) , Insomnia, Seizures and Pre – Operative Sedation.

Chlordiazepoxide and Lorazepam are commonly prescribed Benzodiazepines that differ in their Pharmacology despite having a similar mechanism of action.[89]

Classification of Benzodiazepines[89]

I. Hypnotics

Ex:- Diazepam, Flunazepam, Nitrazepam, Triazolam.

II. Anti – Anxiety

Ex:- Diazepam, Chlordiazepoxide, Oxazepam, Lorazepam, Alprazolam.

III. Anti – Convulsant

Ex:- Diazepam, Lorazepam, Clonazepam, Clobazam

LORAZEPAM

Lorazepam is a Benzodiazepine medication approved by the US food and drug administration (FDA) for short-term relief of anxiety symptoms associated with anxiety disorder, anxiety related insomnia, and treatment of status epileptics.

Off-label use of lorazepam includes rapid tranquilization of agitated patients, alcohol withdrawal delirium and syndrome.[89,91]

- **DOSE[89,100]**

Table No. 13: Dose of Lorazepam.

SL. No	AGE GROUP	INDICATION	DOSE	FREQUENCY
1	Neonates (<1 month)	Seizure, Sedation	0.05 mg/kg	Single dose
2	Infants (1-2 months)		0.5 – 1 mg/kg	
3	Children (2 -12 years)	Anxiety, Sedation	2 mg	OD/BD
4	Adolscents (12 – 18 years)	Anxiety, Insomnia	1 – 3 mg	OD
5	Adults (18 – 65 years)	Anxiety, Epilepsy	1 – 4 mg	OD
6	Elders (>65 years)	Anxiety , Insomnia	0.5 – 1 mg	OD /BD

- **Dose of Lorazepam in Alcohol Dependence and Withdrawal Syndrome**

Table No. 14: Dose of Lorazepam in ADS & AWS.

SL. No	ADS / AWS	SEVERITY	DOSE
1	Alcohol Dependence Syndrome	Mild	2 mg
		Moderate	2 mg to 4 mg
		Severe	4 mg
2	Alcohol Withdrawal Syndrome	Mild	1 – 2 mg
		Moderate	2 mg
		Severe	2 – 4 mg

➢ DOSAGE FORMS & ROA:[89,100]

Table No. 15: Dosage forms and ROA of Lorazepam.

SL. NO	DOASGE FORM	STRENGH	ROA
1	Tablet	0.5 mg, 1 mg, 2 mg	Oral
2	Injection	2 mg/ml, 4 mg/ml	IV/IM
3	Oral Solution	2 mg/ml	Oral

➢ PHARMACOKINETICS[89,96,100]

1. Absorption:- Rapidly absorbed after oral administration 90%

 Bioavailability:- Widely distributed, cross BBB & Placenta

2. Distribution

 PPB:- 85 – 90 %

 Vd:- 1.3L/kg

3. Metabolism:- Liver by Glucuronidation

 Metabolites:- No active metabolites are formed

4. **Elimination:-** Urine and Feces

 Half life:- Approximately 10 – 20 hours

➢ MECHANISM OF ACTION[89]

Lorazepam acts by binding to the site on the GABA-A receptor complex in the central nervous system. This binding enhances the inhibitory action of gamma-aminobutyric acid (GABA) by increasing the frequency of opening of chloride ion channels. The increased chloride influx causes hyperpolarization of neurons, leading to reduced neuronal excitability.

In chronic alcohol consumption, alcohol enhances GABA-mediated inhibition and suppresses glutamate (NMDA) activity. Long term use leads to down regulation of GABA receptors ands up regulation of NMDA receptors. Abrupt cessation of alcohol results in central nervous system hyperexcitability, manifest as tremors, anxiety ,seizures, and delirium.

Lorazepam substitutes for missing GABAergic effect of alcohol during withdrawal, thereby reducing CNS hyperactivity, preventing withdrawal seizures, and controlling agitation and anxiety.

DRUG INTERACTIONS:[89]

Table No. 16: Drug Interactions of Lorazepam.

SI. No		INTERACTED DRUG	EFFECT
1	LORAZEPAM INTERACTED WITH	Opioids	Increased Respiratory depression
2		Alcohol	Excessive sedation and Depression
3		CNS Depressants	Additive sedative effect
4		Antipsychotics	Increased sedation
5		Antihistamines	Increased drowsiness

- **ADVERSE DRUG REACTIONS[89]**

- **Common ADR's**

Sedation, Drowsiness, Dizziness, Ataxia, Asthenia (Weakness), Confusion.

- **Serious ADR's**

Apnea, Hypotension, Respiratory Depression, Paradoxical reactions (aggression, agitation) Retrograde amnesia.

- **Dependence potential:-** Lorazepam is a habit-forming benzodiazepine and may produce tolerance and physical dependence. Abrupt discontinuation can result in withdrawal symptoms.
- **Pregnancy and Lactation:-** Lorazepam is classified as pregnancy category D and may cause fetal harm, neonatal respiratory depression , and withdrawal symptoms when used during pregnancy.

➢ CONTRAINDICATIONS[89]

1. Hypersensitivity to BZD
2. Glaucoma patients
3. Severe Respiratory Insufficiency
4. Severe Hepatic Impairment
5. Myathenia gravis
6. Pregnancy women
7. Lactating mother
8. Alcohol intoxication

➢ USES[92,100]

Lorazepam is used in management of

1. Anxiety
2. Insomnia
3. Alcohol Dependence Syndrome
4. Alcohol Withdrawal Syndrome
5. Epilepsy
6. Pre – Operative Sedation
7. Acute agitation
8. Muscle spasms

CHLORDIAZEPOXIDE

Chlordiazepoxide, it was the first BZD to be used for clinical purpose (1960).It is a long acting BZD commonly used for Psychiatric diseases. It reduces the CNS hyperexcitability, and helps control symptoms like Anxiety, Depression, Tremors, Agitation and Seizures.

The oral absorption is slow and produce a smooth long lasting effect.It is preferred from mild to chronic psychiatric diseases.[89][93]

➢ DOSE[89,100]

Table No. 17: Dose of Chlordiazepoxide.

SL. No	AGE GROUP	INDICATION	DOSE	FREQUENCY
1	Neonants (<1 month)	Not recommended		
2	Infants (1-2 months)	Severe anxiety	0.25 - 0.5 mg/kg	2 – 3 divided doses / day
3	Children (2 -12 years)	Anxiety & Behavioual disturbances	5 – 10 mg	
4	Adolscents (12 – 18 years)	Anxiety & Agitation	10 – 20 mg	3 – 4 divided doses / day
5	Adults (18 – 65 years)	Anxiety & Preoperative anxiety	25 – 100 mg	BD / TID
6	Elders (>65 years)	Anxiety & Mild Withdrawal	5 – 10 mg	BD / TID

		symptoms		

- **Dose of Chlordiazepoxide in Alcohol Dependence and Withdrawal Syndrome[96]**

Table No. 18: Dose of Lorazepam in ADS & AWS of Chlordiazepoxide.

SL.No	ADS / AWS	SEVERITY	DOSE
1	Alcohol Dependence Syndrome	Initial detoxification	50 – 100 mg
		Stabilization	23 mg – 50 mg
		Tapering	10 – 25 mg
2	Alcohol Withdrawal Syndrome	Mild	25 mg
		Moderate	50 mg
		Severe	76– 100 mg

➢ DOSAGE FORMS & ROA[89]

Table No. 19: Dosage forms and ROA of Chlordiazepoxide.

SL. NO	DOASGE FORM	STRENGH	ROA
1	Tablet	5 mg, 10 mg, 25 mg	Oral
2	Injection	100 mg vial (rare)	IV
3	Capsule	5 mg, 10 mg, 25 mg	Oral

➢ PHARMACOKINETICS :- [95][89]

1. Absorption :- Rapidly absorbed after oral administration

i. Bioavailability:- 100%

2. Distribution:- Widely distributed, cross BBB & Placenta

ii. PPB:- 85 – 95 %

3. Metabolism:- Liver (Hepatic metabolism)

iii. Metabolites:- Desmethyldiazepam, Demoxepam

4. Elimination:- Urine and Feces

iv. Half life:- Metabolites: 36 – 200 hours

➢ MECHANISM OF ACTION[89,94]

It exerts its pharmacological action by enhancing the activity of gamma- aminobutyric acid (GABA)**,** which is the major inhibitory neurotransmitter in the brain. Chlordiazepoxide binds to the benzodiazepine binding site on the GABA(A) receptor complex located on neuronal cell membranes. This binding does not directly activate the receptor but increases the affinity of GABA for its receptor**,** thereby potentiating the inhibitory effects of GABA.

When GABA binds to the GABA(A) receptor, it opens chloride ion (Cl^-) channels, allowing

chloride ions to enter the neuron. Chlordiazepoxide enhances this process by increasing the frequency of opening of these chloride channels**.** The influx of chloride ions leads to hyperpolarization of the neuronal membrane**,** making the neuron less excitable and reducing the likelihood of action potential generation.

As a result, neuronal activity in the central nervous system is suppressed.Through this mechanism, chlordiazepoxide produces several therapeutic effects including anxiolytic, sedative, hypnotic, anticonvulsant, and muscle relaxant actions**.** In patients with alcohol withdrawal syndrome, it helps reduce symptoms such as agitation, tremors, anxiety, and seizures by stabilizing neuronal activity and enhancing inhibitory neurotransmission in the brain.

➢ DRUG INTERACTIONS[89]

Table No. 20: Drug Interactions of Chlordiazepoxide.

SL. No	CHLORDIAZEPOXIDE INTERACTED WITH	INTERACTED DRUG	EFFECT
1		CYP 450 Enzyme Inducers	Reduced effectiveness of drug
2		CYP 450 Enzyme Inhibitors	Increased Plasma drug concentration of Chlordiazepoxide
3		CNS Depressants	Increased Respiratory depression

➢ ADVERSE DRUG REACTIONS[89]

- **Common ADR's**:- Sedation, Drowsiness, Fatigue, Dizziness, Ataxia, Impaired Psychomotor performance
- **CNS effects** :- Confusion, Cognitive impairment , Anterograde amnesia
- **Paradoxical reactions** :- Excitement, Agitation, Aggression , Insomnia
- **Severe ADR's :-**Respiratory depression, Hypotension, Blurred vision

➢ CONTRAINDICATIONS[89]

1. Hypersensitivity to BZD
2. Sleep apnea syndrome
3. Severe Respiratory Insufficiency
4. Glaucoma patients
5. Myathenia gravis
6. Pregnancy women
7. Lactating mother
8. Alcohol intoxication

➢ USES[92,100]

1. Drug of choice for the Alcohol Withdrawal Syndrome
2. Prevent Withdrawal Seizures and Delirium remens
3. Less frequent dosing required due to long halflife
4. Effective anxiolytic and sedative
5. Prolonged therapeutic effect
6. Used for Muscle spasms and Preoperative Sedation
7. Anxiety

REVIEW OF LITERATURE

1. **Dr. Nitishkumar D Tank** et.al. conducted a study on **"An observational comparative study of clinical efficacy and safety of chlordiazepoxide and lorazepam in alcohol withdrawal syndrome".** It is a observational prospective and comparative study. Benzodiazepines such as Chlordiazepoxide, Lorazepam and Diazepam are the drugs used mainly in Alcohol Withdrawal Syndrome. These are belongs to same class but have different pharmacokinetic action. Lorazepam and Diazepam are short acting agent with no active metabolites whereas Chlordiazepoxide is long acting agent and convert into active metabolites in Liver. This study conducted in 100 male patients of Alcohol Withdrawal Syndrome [AWS]. They received either Chlordiazepoxide or Lorazepam and divided into two comparison groups while screening. The assessing was done by using the Clinical Institute Withdrawal Assessment for Alcohol scale, revised [CIWA-Ar] in both groups and Clinical Global Impression [CGI] score was also used to evaluate drug efficacy in both groups. The results obtain from CIWA-Ar, CGI-S (Severity) and CGI-I (Improvement) score shows statistical significant difference between two groups but percentage reduction in scale scores were almost similar in both groups. Intra group comparison at different duration of treatment progressed and in between days of treatment there was statistically significant reduction of these scores. No adverse events was reported. The conclusion is both the drugs had almost similar efficacy in terms to reduce CIWA-Ar and CGI-S scores, CGI-I score was reduced and similar safety profile. [101]

2. **Sirjana adhikari**, et.al. conducted a study on **"Cognitive dysfunction in patients with alcohol dependence syndrome in a tertiary hospital Kathmandu"**. The aim of this srajani tudy to find cognitive dysfunction in ADS patients and to identify clinical factors influencing these deficits, It a descriptive observational study was conducted on 62 patients with alcohol dependence recruited from inpatient psychiatric services using

convenient sampling. cognitive functioning was assessed after completion of detoxification using the severity of alcohol dependence questionnaire, frontal assessment battery, and PGI memory scale. The mean duration of alcohol consumption was 13.9 years, with most patients having a moderate level of dependence. Executive dysfunction was observed in 33.9% of patients, mainly affecting conceptualization, programming, and mental flexibility, with period of dependence and education being significant predictors. Memory dysfunction was present in 54.8% of patients, particularly involving visual retention, remote memory, verbal retention, and delayed recall. Age and duration of alcohol consumption were significant predictors of memory impairment. The study concluded that cognitive dysfunction are common in alcohol dependence, highlighting the need for routine neuropsychological assessment for early identification and rehabilitation.[102]

3. **Channaveerachari Naveen Kumar** et.al conducted a study on **Randomized double-blind comparison of lorazepam and chlordiazepoxide in patients with uncomplicated alcohol withdrawal**

The main aim of this study is to compare the efficacy of lorazepam and chlordiazepoxide in the management of uncomplicated alcohol withdrawal syndrome .A randomized double-blind comparative clinical trial was conducted in 100 male inpatients with moderately, severe, uncomplicated alcohol withdrawal syndrome. Participants were randomized to receive either lorazepam[8mg/day] or chlordiazepoxide[80mg/day],tapered over 8 days and withdrawal severity was assessed using the revised Clinical Institute Withdrawal Assessment for Alcohol scale .Both drugs shoed comparable efficacy in reducing alcohol withdrawal symptoms .Irritability and dizziness were more common with lorazepam ,while palpitations were more frequent with chlordiazepoxide in managing uncomplicated alcohol withdrawal and may be preferred in patients with liver dysfunctions.[103]

4. **March et.al** conducted a **Comparative study on Lorazepam vs Chlordiazepoxide for the treatment of alcohol withdrawal syndrome and prevention of delirium tremens in general medicine ward patients**. Out of 2112 patients screened ,142 met inclusion criteria[lorazepam=74,chlordiazepoxide=68]. There was significant difference in the incidence of delirium tremens between the two groups[7% vs 9%].There were no significant differences in duration of the treatment, length of hospital stay or benzodiazepine related adverse events. However patients treated with chlordiazepoxide

required significantly higher doses of adjunctive benzodiazepines for symptom control. The study concluded that both lorazepam and chlordiazepoxide are equally effective in preventing delirium tremens in patients with alcohol withdrawal syndrome admitted to general medicine wards, although chlordiazepoxide may necessitate additional supportive therapy.[104]

5. **Ranjani Ramanujam** et.al. conducted study on **A comparative study of the clinical efficacy and safety of lorazepam and chlordiazepoxide in alcohol dependence syndrome.** The main aim to this study to find out the efficacy and safety of the lorazepam and chlordiazepoxide in the ADS patients. It is a prospective, randomized, double-blind comparative study to evaluate the clinical efficacy and safety of lorazepam and chlordiazepoxide in patients with alcohol dependence syndrome (ADS) presenting with mild to moderate alcohol withdrawal symptoms. The study was carried out at a teaching hospital in Bangalore and included 60 patients aged above 18 years, who were randomly allocated into two equal groups. One group received lorazepam (8mg/day) and the other chlordiazepoxide (80mg/day), with doses gradually tapered over 8 days. The severity of alcohol dependence was assessed using the severity of alcohol dependence questionnaire (SADQ), while withdrawal symptoms were quantified using the CIWA-Ar scale. Liver function tests were evaluated at baseline and at the end of the study to assess safety.The results showed a significant reduction in CIWA-Ar scores with in both groups over the study period, indicating effective control of withdrawal symptoms. However, no significant difference was observed between the lorazepam and chlordiazepoxide groups in terms of efficacy or liver function parameters. The authors concluded that the lorazepam is non-inferior to chlordiazepoxide in managing alcohol withdrawal symptoms and can be considered a safe and effective alternative, especially in patients with potential hepatic impairment.**[105]**

6. **De Ternay** et.al., conducted a cross sectional observational study on **Insufficient physical activity is a global marker of severity in Alcohol Use Disorder**. The main aim of the study is to evaluate whether insufficient physical activity could act as a global marker of severity in patients with Alcohol Use Disorder (AUD). The study included 382 treatment seeking AUD patients, in whom physical activity levels were assessed using International Physical Activity Questionnaire (IPAQ). Based on Physical Activity (PA) levels, participants were categorized into insufficient PA and sufficient PA groups. The

severity of alcohol use disorder was assessed using multiple standardized instruments, including DSM – 5 diagnostic criteria, the Alcohol Use Disorder Identification Test (AUDIT), and the Severity of Alcohol Dependence Questionnaire (SADQ). Logistic regression analysis was used to examine associations between physical activity levels and clinical, psychological, and behavioral parameters. The study found that patients with insufficient physical activity has significantly high Body Mass Index, a greater number of DSM – 5 AUD criteria, and increased opioid use. They also demonstrated higher levels of nicotine dependence, anxiety, impulsivity and poor sleep quality as measured by Fagerstrom Test for Nicotine Dependence, State – Trait Anxiety Inventory, Impulsivity Scale, and Pittsburgh Sleep Quality Inventory respectively. Additionally these patients reported significantly lower quality of life scores on the WHO quality of life scale. [106]

7. **Hisham Laswi** et.al., conducted a study on "**Trends of Alcohol Withdrawal Delirium in the Last Decade: Analysis of the Nationwide Inpatient Sample"**. It is a retrospective study. The main aim of the study is the nationwide In patient sample to examine the trends of alcohol withdrawal delirium in the period 2010 – 2019. Approximately half of the patients with Alcohol use disorder experience withdrawal symptoms such as hallucinations, seizures, delirium in USA. We searched the data bases for hospitalizations using the ICD codes (291.0 and F10231). We involves all participants complicated by AWD and hospitalizations. The result is about the millions of AWD per million hospitalizations increased from 2671 in 2010 and 3405 in 2109, with an Annual Percentage Change (APC) of 3.1. Similarly AWD admission rate per million hospitalizations increased from 1039 inpatient mortality. THC and LOS over the studied period. In general, females gender, younger age and black race were associated with better clinical outcomes. The conclusion of the study is showed that an increase and admission rates of AWD. Mortality, LOS and THC increased over the study period. Younger age, female gender and Black race were associated with better clinical outcomes. [107]

8. **Carrissa Gardiner** et.al., conducted a study on **"The effect of alcohol on subsequent sleep in healthy adults : A systematic review and meta – analysis".** The main aim of the study is to examine the effects of alcohol consumption on night-time sleep characteristics with particular focus on dose and timing of intake. A total of 27 were included in 2/11/2026the analysis. The findings demonstrated significant alterations in the sleep architecture following alcohol intake .Alcohol consumption resulted in a delay

in REM sleep onset and reduction in REM sleep duration. A clear dose-response relationship was observed, where even a low dose of alcohol negatively affected REM sleep and disruption progressively worsened with higher doses. High doses of alcohol were associated with reduced sleep onset latency and shorter latency to deep sleep. However this initial sedative effect appeared to worsen later REM sleep disruption. The effects of alcohol on total sleep time, sleep efficiency, and wake after sleep onset showed considerable variability and uncertainty. The authors concluded that even low doses of alcohol impairs REM sleep whole higher doses may temporarily shorten sleep onset but lead to greater overall sleep disturbance.[108]

9. **Ritwik Mishra** et.al, conducted a study on **"Cognitive Impairment in Alcohol Dependence Syndrome : A cross sectional study using MoCA"**. The main aim of the study is to asses cognitive functioning in patients with Alcohol Dependence Syndrome (ADS) and examine the relationship with socio – demographic and clinical factors. ADS leads to not only physical and psychological complications but also considerable cognitive impairment, which is frequently under recognized in routine clinical practice. Early detection of cognitive dysfunctions crucial for planning appropriate interventions and enhancing treatment compliance. It is a cross – sectional observational study was carried out among 110 male in patients with a diagnosis of ADS at a tertiary care hospital in Western India. Cognitive function was evaluate by using Montreal Cognitive Assessment (MoCA), where scores below 26 were considered indicative of cognitive impairment. Socio demographics and clinical details were obtained using a semi – structured questionnaire. Data were analyzed using chi – square tests and independent t – tests . Cognitive impairment was identified in 21 (19.1%) participants. The domains most significantly affect were attention, visuospatial / executive functioning and delayed recall ($p < 0.01$). A statistically significant association was observed between longer duration of alcohol use and cognitive impairment($p = 0.025$), with increased prevalence among individuals consuming alcohol for over 20 years . Although impairments was more common in patients with lower educational levels, the association did not reach statistical significance ($p = 0.102$) . No significant differences were noted in language and abstraction domaians.The conclusion of the study is A notable proportion of patients with ADS demonstrate early cognitive dysfunction particularly those with prolonged alcohol consumption. Incorporating routine cognitive assessment using instruments such as MoCA into standard clinical practice may assist in developing personalized treatment

and rehabilitation plans.[109]

10. **Alyssa T Brooks et** al conducted a study on "**The effectiveness of behavioral therapies, including cognitive-behavioral therapy for insomnia, in managing sleep disturbances among individuals with alcohol related disorders**". It is a systematic review aimed at evaluating the existing evidence on behavioral sleep interventions in thus population. The study involved a comprehensive search of four electronic databases-Pubmed, PsycINFO, Embase and CINAHL Plus- which yields six studies that met the inclusion criteria. The included articles were assessed using Cochranes Grades Of Recommendation, Assessment, Development and Evaluation [GRADE] scoring system .Improvements were noted in treatment groups compared to controls, indicating the potential benefits of non pharmacological sleep interventions. However the number of eligible studies was limited, suggesting that such interventions are under-researched among individuals with alcohol-related disorders. The review concluded that although behavioral therapies appear effective in improving sleep outcomes, further well-designed and mixed-methods studies are required to better understand patient experiences and to develop acceptable and targetted sleep interventions for this population.[110]

11. **Ian Cornel** Et al conducted a study on "**The effects of acute and chronic alcohol consumption on sleep architecture and neurophysical parameters"**. It is a narrative review study examining the interaction between alcohol and neurotransmitters systems involved in sleep regulation, The study described the acute administration of large amounts of alcohol before sleep reduces sleep onset latency and alters sleep architecture during the early part of the night when blood Alcohol levels are high, followed by disrupted and poor-quality sleep later in the night. Chronic alcohol abuse and dependence were found to be associated with persistent sleep disturbances, reduced slow wave sleep and increased rapid eye movement sleep even during prolonged abstinence. These alterations maybe contribute to increase risk of relapse .Te review also highlighted development of tolerance with repeated alcohol use and discussed possible underlying neurochemical mechanisms. Sex differences, effects on sleep homeostasis, and circadian rhythm disturbances were addressed. Additionally sleep disruption during adolescence was identified as a potential risk factor for the development of alcohol dependence.[111]

12. **Koob and Colrain** conducted a study on "**The relationship between alcohol use disorder and sleep disturbances within a theoretical narrative review framework**

based on the feed forward all static model of addiction". The study aimed to explain how sleep disturbance interact and contribute with the development and maintenance of AUD across its three-stage addiction cycle: binge/intoxication ,withdrawal/negative effect, and anticipation. During the intoxication stage, alcohol reduces sleep onset latency but leads to poor sleep quality and increased wakefulness later I that night, primarily due to its effects on GABAergic and dopaminergic systems. In the withdrawal, decreased a low-wave sleep and partial REM recovery are observed, with limited improvement in sleep disturbances within the first 30 days of abstinence. Neurobiological mechanism include reduced GABA receptor modulation, decreased dopamine activity and over activity of stress related neuromodulators such as corticotrophin-releasing factor, norepinephrine and cytokines. During the preoccupation, persistent sleep disturbances are noted even in long term abstinent individuals including prolonged sleep latency reduced slow wave cycle sleep decreased delta EEG activity and increased REM sleep. Glutamatergic dysregulation is proposed as a contributing factor to these chronic sleep abnormalities. The study concluded that sleep pathology and AUD pathology reinforce each other in a feed forward manner, contributing to an allostatic load that perpetuates the addiction cycle.[112]

13. **HH LIN NGUI et al** conducted a study on "**The clinical management of alcohol withdrawal syndrome and medically assisted withdrawal".** It is a clinical narrative review focusing on key aspects of management special population considerations, and emerging treatment strategies. The review highlights that nearly 50% of individuals with the long-term heavy alcohol use develop AWS upon significant reduction of alcohol intake, and severe cases may be life threatening. Medically assisted withdrawal is often the initial step in the treatment pathway for AUD. The review discusses important components of MAW, including monitoring, pharmacological management and modification required for vulnerable groups such as pregnant women and older adults. Benzodiazepines are identified as the mainstay of treatment with strong evidences supporting their efficacy in reducing withdrawal severity and preventing complications. However concerns regarding abuse potential, cognitive impairment drug interactions delirium dementia risk and sleep disturbances are emphasized. Given the role glutamergic over activity in alcohol withdrawal anti-glutamergic treatment strategies are discussed as potential therapeutic alternatives. The review concluded that while benzodiazepines remain the standard off care in MAW, safer and more targeted

approaches are needed to improve outcomes and reduce adverse effects in patients undergoing alcohol withdrawal. [113]

14. **Liu et al** conducted a study to "**Investigate factors related to sleep disturbances during the acute withdrawal period in patients with the Alcohol use disorder."** It is a comparative observational study involving 50 male AUD patients aged 18-66 years and 50 healthy male controls. On days 1-2 of alcohol withdrawal sleep architecture and related architecture and related breathing parameters were assessed using polysomnography. Psychological and clinical parameters were evaluated using the Pittsburgh Sleep Quality Index, Beck Depression Inventory, Penn Alcohol Craving Scale and Barat Impulsiveness Scale. Compared to controls AUD patients demonstrated significantly reduced total sleep time, lower sleep efficiency decreased REM sleep and increased snoring frequency and duration. They also showed significantly higher vs cores for alcohol craving, depressive symptoms and anxiety were significantly associated with poor sleep quality. The study concluded that significant sleep disturbances occur during the acute withdrawal phase of AUD and are strongly influenced by craving and mood disturbances. [114]

15. **Kashyap Shah** et.al conducted a study on **"Assessment of cognitive functions in patients with Alcohol Dependence disorder and its implications for primary care : A cross – sectional study".** The main aim of the study is to evaluate the cognitive impairment in patients with ADS and to examine the relationship between the severity of the Alcohol dependence and the degree of cognitive dysfunction among inpatients in a tertiary care hospital. It is a hospital based cross sectional study. The study was conducted among 90 patients diagnosed with alcohol dependence. Cognitive function was evaluated by using standardized tools including Montreal Cognitive Assessment (MoCA) , Frontal Assessment Battery (FAB) and Severity of Alcohol Dependence Questionnaire (SADQ).Individuals with severe alcohol dependence demonstrated markedly reduced cognitive function reflected by low scores in MoCA and FAB scales. Approximately 72.2% of participants scores below the cutoff of MoCA, while 33.3 % fell below FAB cutoff, indicating substantial Cognitive function. A significant negative correlation was observed between SAD – Q scores and both MoCA (-0.059) and FAB (-0.324) scores, suggesting increasing severity of Alcohol dependence is linked with worsening cognitive impairment. The conclusion of the study is ADS is strongly associated with significant

cognitive deficits, particularly affecting executive and frontal lobe functions. Implementing regular cognitive assessment protocols in primary care can facilitate early identification, targeted intervention, and improved overall patient prognosis, thereby reducing the long term healthcare burden of alcohol related disorders. [115]

16. **Alison mary** et.al., conducted a study on**"The effect of alcohol withdrawal syndrome severity on sleep, brain, and cognitive"**. The main aim of the study is to evaluate sleep disturbances structural brain alternative and neuropsychological defects observed in early abstinence patients. It is a observational cross-sectional study was conducted on 54 patients with alcohol use disorder in early abstinence (4-21 days) and compared them with 50 healthy controls. After the resolution of acute physical withdrawal symptoms, participants underwent detailed neuropsychological assessment, T_1 weighted magnetic resonance imaging and polysomnography in a subgroup of patients. Based on the severity of withdrawal symptoms during the acute phase patients were categorized into mild alcohol withdrawal syndrome (Cushman score ≤4 , without benzodiazepine)and moderate alcohol withdrawal syndrome (Cushman score >4 with benzodiazepines), while patients with severe complaints such as delirium tremors /seizures were excluded. Results showed that patients with mild AWS had brain grey matter volume and sleep quality comparable to healthy controls although subtle impairment in processing speed and episodic memory were observed.

In contrast moderate AWS patients exhibited significant alterations in brain structure (wide spread grey matter reduction particularly in the fronto insular cortex and thalamus / hypothalamus regions along with impaired sleep architecture and also poorer short-term memory and lower overall cognitive performance is observed in moderate AWS when compared to mild AWS. [116]

17. **Hwang in cheol**et.al., conducted a study on **"Association between alcohol consumption and sleep difficulty in a nationwide Korean Survey".** The main aim of the study is to investigate the association between drinking patterns and sleep related difficulties among Korean adults. The data were obtained from 4,937 adults who participated in 2019 Korea National Health and Nutrition Examination Survey and provide information on both sleep problems and alcohol consumption. Overall, 8.5% of participants reported experiencing substantial sleep difficulties. The lowest prevalence of sleep problems was observed among individuals who consumed alcohol less than once per week or drank 1 – 2 cups per

occasion, even lower than that seen in non-drinkers. Among those who consumed alcohol, a clear dose – response relationship was identified, with increasing frequency and quantity of alcohol intake associated with higher odds of sleep difficulty. Sub group analyses showed that this linear association was particularly strong in adults younger than 50 years and among women. Alcohol intake is significantly associated with an increased risk of sleep difficulties, with stronger effects observed in younger adults and females. These findings highlight the importance of targeted preventive strategies and further research to better understand the impact of alcohol consumption on sleep health. [117]

18. **Junghanns et al**. conducted a comparative observational study with polysomnographic assessment to examine the impact of chronic and high alcohol consumption on sleep architecture and sleep -related declarative memory consolidation in alcohol-dependent patients during abstinence. The study included 36 alcohol dependent patients, divided into two groups based on duration of abstinence: short term abstainers[approximately 22 days] and long-term abstainers[approximately 116 days].Both groups were comparable in terms of age, duration of alcohol dependence, and daily alcohol consumption prior to treatment. Participants underwent learning tasks before sleep, which included semantically associated word pairs, a face-name association task to asses declarative memory, a mirror tracing task to evaluate procedural memory. Sleep was recorded using overnight polysomnography and memory retention was assessed the following morning through cued recall and task repetition. The results showed no significant differences between short term and long term abstinent group in overall sleep parameters. However, across both groups, a longer duration of alcohol dependence was negatively correlated with non-REM sleep and higher pre-abstinence alcohol consumption was associated with poorer recall performance on the face-name association task. Among long term abstainers, a positive correlation was observed between duration of abstinence and slow wave cycle.[118]

19. **Bird et.al.** (1994) conducted a study on to evaluate the use of the benzodiazepines in the management of alcohol withdrawal syndrome (AWS) and critically assess whether lorazepam can be justified as the first line benzodiazepine for the condition. The main aim of this study to ongoing clinical debate regarding the optimal choice of benzodiazepines in alcohol withdrawal. A comprehensive literature search was perfumed using a online database (BRS colleague).A comparative studies, and case reports

involving chlordiazepoxide, diazepam, and lorazepam. The study assessed the pharmacokinetics, clinical efficacy, safety profile, and duration of action of these drugs in the patients with alcohol withdrawal. Lorazepam undergoes direct glucuronidation without active metabolites and has an intermediate half-life, making it safer in elderly patients and in those with hepatic dysfunction,in contrast, long-acting benzodiazepines such as chlordiazepoxide and diazepam provides smoother withdrawal control because of their longer half-life and self-tapering effect. Symptoms control, prevention of complications such as seizures and delirium tremors, and overall tolerability were evaluated in the included reports. The available evidence did not demonstrate clear superiority of lorazepam over other benzodiazepines in terms of efficacy. No significant differences were consistently observed in clinical conditions. The study concluded that current evidence is insufficient to recommend lorazepam as the routine first line agent for alcohol withdrawal syndrome and emphasized the need for large, well-designed comparative trails.[119]

20. **Horat Gann** et.al. conducted a study on **"Sleep and the cholinergic rapid eye movement sleep induction test in patients with primary alcohol dependence".** The main aim of the study is to evaluate whether sleep parameters, especially rapid eye movement [rem] sleep variables, may serve as predictors for relapse in alcohol dependent patients. the present study investigated by polysomnographically assessed sleep parameters in alcohol dependent patients after withdrawal and in healthy control subjects during base line and after a cholinergic stimulation paradigm. forty patients diagnosed with alcohol dependence were admitted to a specialized deaddiction unit and underwent sleep recording at three different stages 2 to 3 weeks after withdrawal [t0], and during followup at 6 months [t1] and 12 months [t2] after hospital discharge. a sub group of 17 patients underwent a cholinergic rem induction test [crit] at t0 using galanthamine, a reversible cholinesterase inhibitor. two control groups were included for comparison: thirty age and gender matched healthy subjects under baseline conditions, and 17 matched controls for comparison during crit. the results includes that the patients showed significant disturbances of sleep continuity and sleep architecture, including a reduction in slow wave sleep [sws]. additionally, patients showed increased REM sleep pressure, characterized by shortened rem latency, increased REM density and a higher percentage of rem sleep. following galanthamine administration, both patients and control subjects demonstrated significant changes in sleep continuity and architecture, with further

reductions in sws and increases in REM sleep parameters. no significant drug by group interactions were found, except for sws expressed as a percentage of sleep period time. patients who remained abstinent for at least 6 months at follow up exhibited significantly less abnormalities of REM sleep at t0 compared to the group of patients that relapsed at 6 months follow up. [120]

21. **Louise pilon et.al.** conducted a study on **"The relationship between subjective sleep disturbances illness insight in individuals with alcohol related cognitive disorder".** a cross-sectional observational study investigated the association between illness insight and subjective sleep disturbances in individuals with varying degrees cognitive status. the primary aim of the study was to examine whether illness insight is related to subjective sleep disturbances and dysfunctional beliefs about sleep among individuals with aud without cognitive impairment, individuals arc1, and individuals with ks. a secondary aim was to explore the role of illness insight in dysfunctional beliefs and attitudes toward sleep. the study included a convenience sample of 62 participants, comprising 24 individuals with korsakoff's syndrome, 17 individuals with alcohol related cognitive impairment, and 21 individuals with alcohol use disorder without cognitive impairment. illness insight was assessed using the pittsburgh sleep quality index [psqi] and the dysfunctional beliefs and attitudes about sleep [dbas] questionnaire. general cognitive functioning was measured with the montreal cognitive assessment [moca] to characterize cognitive status across groups. the results demonstrated comparable levels of subjective sleep disturbances across all three diagnostic groups, despite marked differences in cognitive functioning and presumed illness insight. importantly, no significant association was found between illness insight and subjective sleep disturbances in any of the groups. additionally, illness insight did not significantly influence dysfunctional beliefs and attitudes about sleep. these results highlight potential limitations of self-report sleep measures in populations with alcohol related disorders and suggest complaints may be influenced by factors other than illness,such as neurological changes, mood disturbances, or chronic alcohol related sleep dysregulation. [121]

22. **Daniel j. Buysse et.al** conducted a study on **"The Pittsburgh Sleep Quality index: a new instrument for psychiatric practice and research".** the pittsburgh sleep quality index [psqi] was developed and validated over an 18-month period to assess sleep quality and disturbances in clinical populations, particularly psychiatric patients who frequently

report sleep complaints. it was a comparative observational cross-sectional study. the main aim of the study was to evaluate the clinimetric and clinical properties of this self-rated questionnaire and determine its ability to distinguish between good and poor sleepers. the study included a total of 168 participants: 52 healthy [good sleepers] 54 patients with depression, and 62 patients with diagnosed sleep disorders. the psqi consists of 19 self- rated items generating seven component scores- subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction- which together yield a global score ranging from 0 to 21. the results demonstrated acceptable internal consistency, good test- retest reliability, and strong validity. a global paqi score greater than 5 showed high diagnostic accuracy, with a sensitivity of 89.6% and specificity of 86.5%, effectively differentiating good and poor sleepers, thereby supporting its usefulness in psychiatric clinical practice and research settings.[122]

23. **Parvinder kaur et.al** conducted a study on **"Effects of abstinence of alcohol on neurocognitive functioning in in patients with alcohol dependence syndrome"**. it is an observational, single- group longitudinal study conducted to examine the effects of abstinence on neurocognitive functioning in patients with alcohol dependence syndrome [ads]. the main aim of the study was to assess changes in neuropsychological functions over a period of abstinence and to explore the correlation between clinical drinking variables and neurocognitive performance. a total of 60 consecutive male patients diagnosed with ads, meeting the inclusion and exclusion criteria, were enrolled. neurocognitive assessments were conducted at three months of abstinence. the results demonstrated significant improvement ($p<0.05$) in all neurocognitive domains across the three assessments, except for visuomotor function, which did not show statistically significant improvement at one month($p>0.05$). significant improvements from baseline to three months were observed in verbal fluency, working memory, set- shifting ability (measured using wcst total and preservative errors), and visuomotor function ($p<0.05$). furthermore, significant interactions were found between drinking history variables-such as duration of use, duration of dependence, average daily intake, and the time since last intake and performance in verbal fluency, working memory, set-shifting, and visuomotor functions ($p<0.05$). the findings indicate that neurocognitive functions improve with sustained abstinence over three months and highlight the importance of early cognitive assessment and intervention in individuals withADS.[123]

AIM & OBJECTIVES

AIM

The main aim of the study is to clinically assess sleep quality and cognitive impairment in patients with alcohol dependence syndrome and to evaluate the relationship between sleep disturbance and cognitive dysfunction

➢ OBJECTIVES

❖ Primary objects

1. To asses the quality of sleep in patients with alcohol dependence syndrome and alcohol withdrawal using standardized clinical tools
2. To evaluate the level of cognitive impairment in alcohol dependent using appropriate cognitive assessment scales.

❖ Secondary objectives

1. To study the association between sleep quality and cognitive impairment in alcohol dependence patients.
2. To identify the prevalence of sleep disturbance among patient with alcohol dependence syndrome.
3. To determine the extent of cognitive dysfunction in alcohol dependence patients.
4. To assess the influence of duration and severity of alcohol use on sleep quality and cognitive function
5. To identify the pattern of sleep problems (insomnia, frequent awakenings, reduced sleep duration, poor sleep efficiency)
6. To assess the extent and domains of cognitive impairment (attention, memory, executive function, orientation)
7. To evaluate the relationship between sleep quality scores and cognitive impairment scores in alcohol dependence patients.
8. To analysis the relationship between severity of alcohol dependence and cognitive dysfunction. The main aim of the study is to clinically assess sleep quality and cognitive impairment in patients with alcohol dependence syndrome and to evaluate the relationship between sleep disturbance and cognitive dysfunction

METHODOLOGY

- **STUDY DESIGN:-** Observational study
- **STUDY SITE OR PLACE:- District Hospital, Proddutur**
- **STUDY DURATION:-** This study was conducted for 6 months, during the year 2025-2026
- **SAMPLE SIZE:-** The sample size was 120

- **STUDY CRITERIA**

❖ **Inclusion criteria**

- Patients who are willing to participate in the study
- Patients diagnosed with alcohol dependence/ alcohol withdrawal syndrome
- Patients age with above 25 years

❖ **Exclusion Criteria**

- Patients with other psychiatric disorders
- Patients with severe medical conditions affecting cognition
- Non-cooperative patients

- **STUDY TOOLS**

- **Pittsburgh Sleep Quality Index (PSQI)** – for sleep quality
- **Mini-Mental State Examination (MMSE)** – for cognitive function
- **Clinical Institute Withdrawal Assessment for Alcohol (Revised) scale (CIWA –Ar)–** for Withdrawal of alcohol
- **Severity of Alcohol Dependence Questionaire (SADQ)–** for Dependence of Alcohol
- Structured questionnaire for demographic and clinical data

- **DATA COLLECTION METHOD**

- Interview-based questionnaire
- Clinical records review
- Sleep and cognitive tests performed during assessment

- **METHOD**

1. This observational study was conducted in government hospital after approval from the institutional ethical committee (SLVP 2025-2026), Sri Lakshmi Venkateswara Institute of Pharmaceutical Sciences.

2. After informing about the purpose and details of study, patient informed consent was obtained by direct patient interview.
3. A specially designed proforma was used for collecting data

RESULTS

A Comparative Observational Study was conducted for 6 months in Psychiatry Department of Andhra Pradesh Vaidhya Vidhana Parishadh – District Hospital ,Proddutur. During the study period over a120 cases of Alcohol attributed patients were considered who comes under inclusion criteria.

Demographic details

1. Distribution Based on Age Group

According to different age groups. The majority of patients were in the 31-40 years age group [46.6%], followed by the 41-50 years group [37.5%] , the 20-30 years group accounted for [6%], while [10%] were in the 51-60 years group. Only [0.8%] of patients belonged to the 61-70 years group.This shows that most patients were in the 31-40 years age group.

Table No. 21: Distribution Based on Age Group.

SL.No	Age group	No. of Patients	Percentage (%)
1	20-30 years	06	6%
2	31-40 years	56	46.6%
3	41-50 years	45	37.5%
4	51-60 years	12	10%
5	61-70 years	01	0.8%

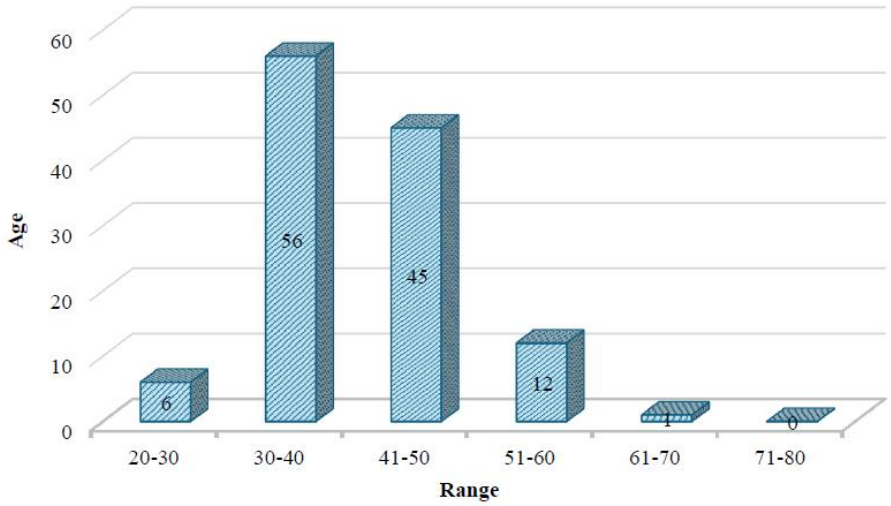

Figure No. 10: Distribution based on different age group.

2. Distribution Based on Education

According to the education wise distribution 120 patients, while 111patients [92.5%] were educated , while 9 patients [7.5%] were uneducated. The results show that the majority of patients were educated, with only small proportion being uneducated. This indicates that most participants in the study had some level of education.

Table No. 22: Distribution Based on Education.

SL. No	Education	No.of Patients	Percentage (%)
1	Educated	111	92.5%
2	Uneducated	09	7.5%

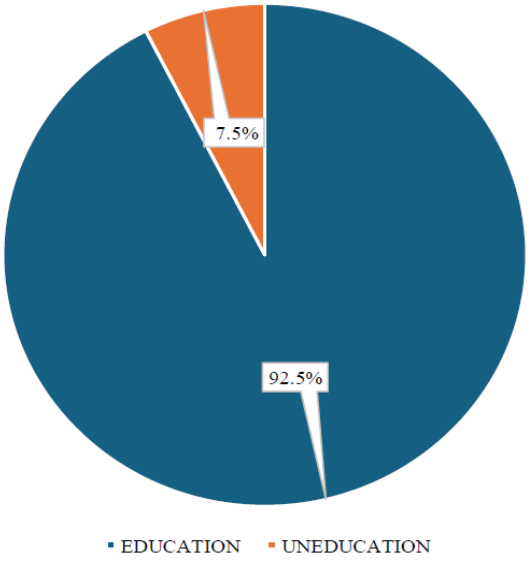

Figure No. 11: Distribution Based on Education.

3. Distribution Based on Duration of Alcohol Intake

According to duration of alcohol intake the patients are divided as 0-5 years [08 patients], 6-10 years [27 patients], 11-15 years [38 patients], 16-20 years [23 patients], >21 years [12 patients] and the percentage are 8%, 25%, 35%, 21%, 11% respectively.

Table No. 23: Distribution Based on Duration of Alcohol Intake.

Sl. No	Duration of alcohol intake	No. of patients	Percentage
1	0-5 years	08	8%
2	6-10 years	27	25%
3	11-15 years	38	35%
4	16-20 years	23	21%
5	>21 years	12	11%

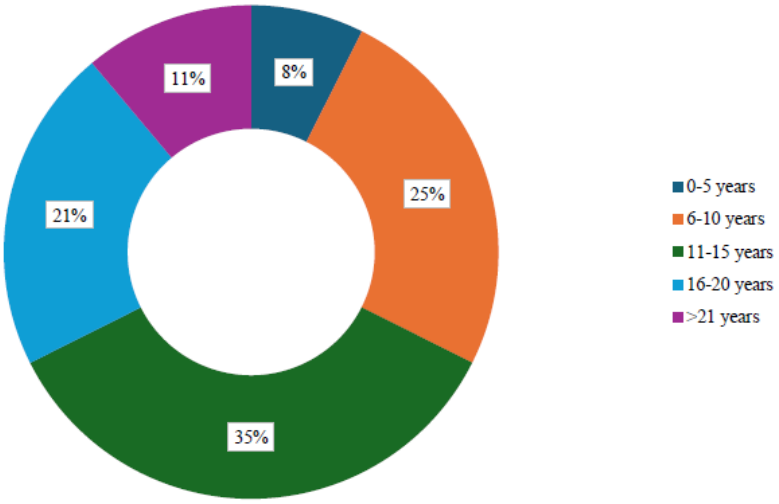

Figure No. 12: Distribution Based on Duration of Alcohol Intake.

4. Distribution Based on Married Status

According to married status , 119 patients [92.5%] were married, while 9 patients [7.5%] were unmarried. The results indicated that the majority of the patients were married, with only a small proportion being unmarried.

Table No.24: Distribution Based on Married Status.

Sl. No	Married status	No. of Patients	Percentage
1	Married	111	92.5%
2	unmarried	09	7.5%

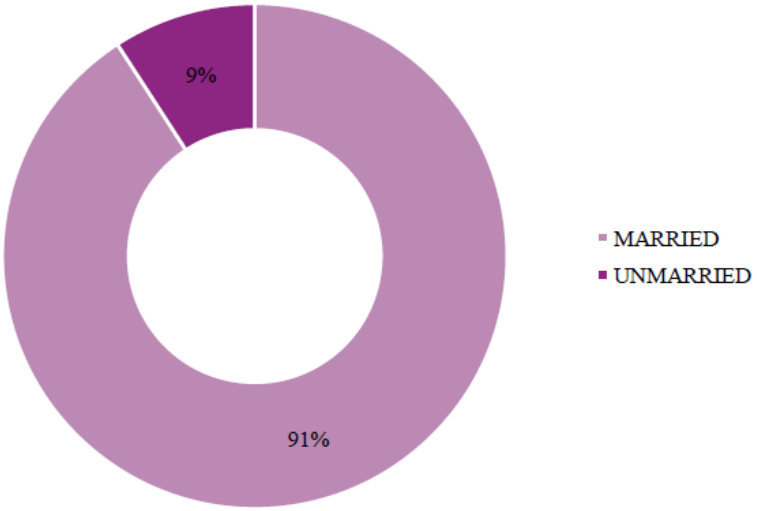

Figure No. 13: Distribution Based on Married Status.

5. Distribution Based on Type of Alcohol

According to Distribution Based on Type of Alcohol intake there are mainly 33.33% of

patients intake Whisky as their daily alcohol consumption while only 0.83 % of patient intake Beer and Brandy then upto 11.67% of Liquor, 10 % of Beer, 10% of Beer and Whisky, 9.17% of Brandy, 8.33% of Whisky and Liquor, 7.50% of Brandy and Whisky, 5% of people consume other brands such as Manshion House, Vodka etc 4.17 % of people consume more than two brands as their daily consumption of Alcohol

Table No. 25: Distribution Based on Type of Alcohol Intake.

Sl. No	Type of alcohol	No. of Patients	Percentage
1	Brandy	11	9.17%
2	Beer + brandy	1	0.83%
3	Beer	12	10%
4	Beer + whisky	12	10%
5	Whisky	40	33.33%
6	Whisky + liquor	10	8.33%
7	Liquor	14	11.67%
8	Brandy + whisky	9	7.50%
9	>2 brands	5	4.17%
10	Other brands	6	5%

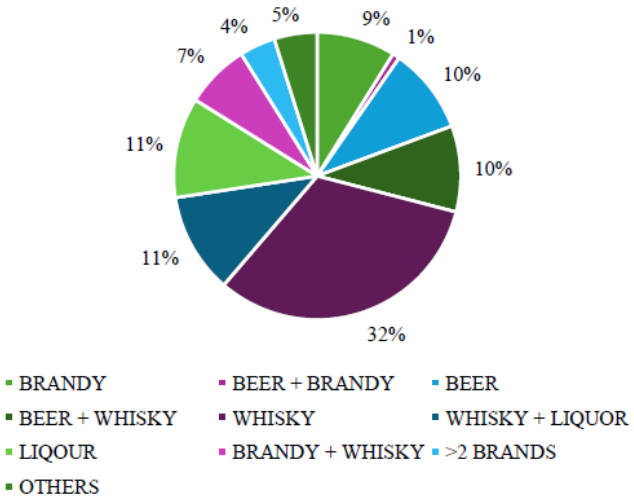

Figure No. 14: Distribution Based on Type of Alcohol Intake.

6. Distribution Based on Other Addiction

The distribution was analyzed based on other addictions. Among them , 79 patients [65.8%] had addiction, while 16 patients [13.3%] had occasional addiction, and 25 patients [20.8%] reported on addiction. The results indicate that the majority of patients had some form of addiction.

Table No. 26: Distribution Based on Other Addiction.

Sl. No	Other addictions	No. of Patients	Percentage
1	Addiction	79	65.8%
2	Occasional addiction	16	13.3%
3	No addiction	25	20.8%

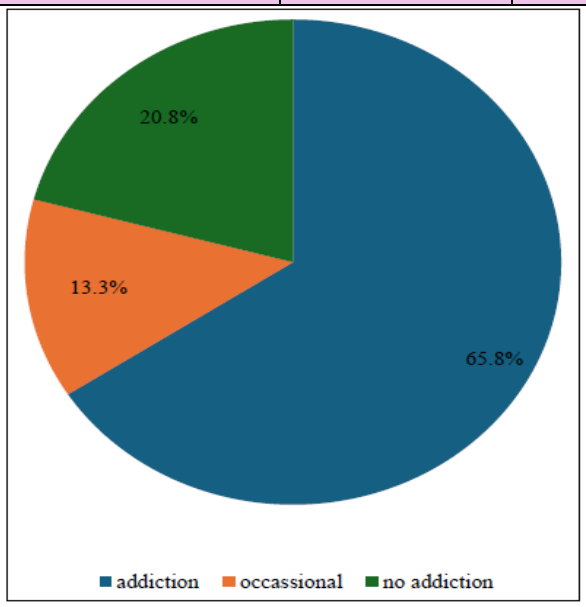

Figure No. 15: Distribution Based on Other Addiction.

7. Distribution Based on Quantity

According to their alcohol consumption was analyzed based on quantity.among them, 26 patients [21.7%] consumed 90-180 ml, while 48 patients [40%] consumed 180-360ml. 46 patients [38%] consumed more than 360 ml. The result show that the majority of patients consumed 180-360 ml of alcohol.

Table No. 28: Distribution Based on Quantity of Alcohol Intake.

Sl. No	Quantity	No. of Patients	Percentage
1	90-180 ml	26	21.7%
2	180-360 ml	48	40%
3	>360 ml	46	38%

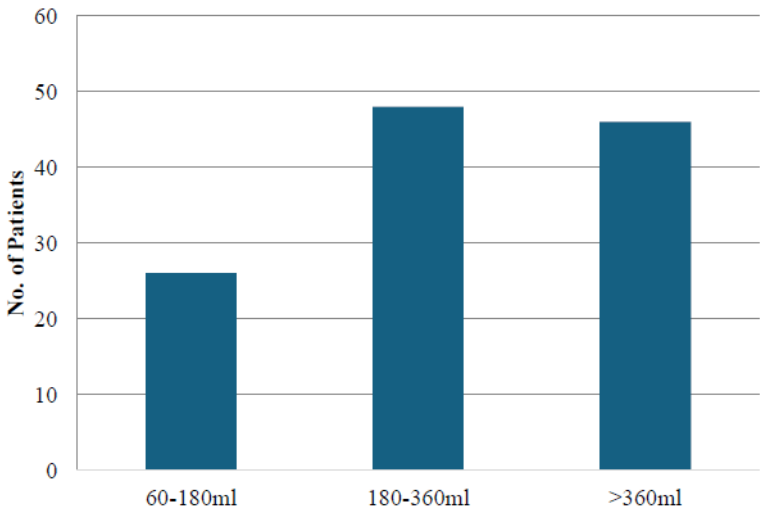

Figure No. 16: Distribution Based on Quantity of Alcohol Intake.

8. Distribution Based on Severity Alcohol Dependence Syndrome

According this distribution was analyzed based on alcohol dependence syndrome severity. Among them, 24 patients [20%] had mild dependence , 54 patients [45%] had moderate dependence, and 42 patients [35%] had severe dependence. The results show that the majority of patients had moderate alcohol dependence syndrome.

Table No. 29: Distribution Based on Severity Alcohol Dependence Syndrome.

Sl. No	Severity of ADS	No. of Patients	Percentage
1	Mild	24	20%
2	Moderate	54	45%
3	Severe	42	35%

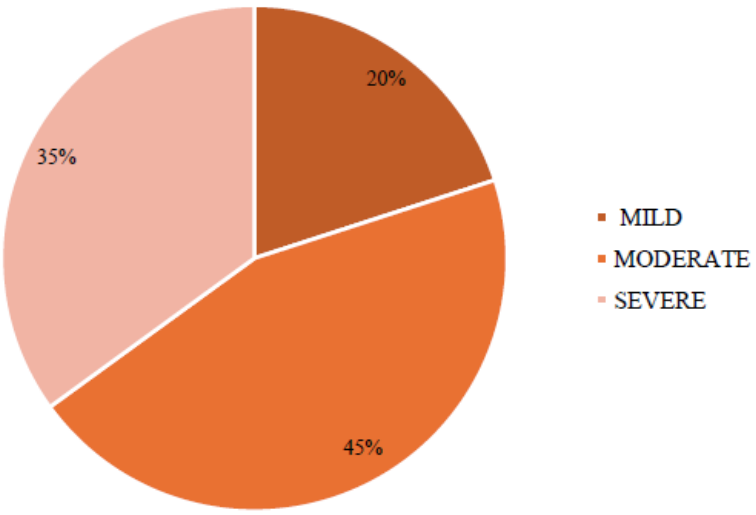

Figure No. 17: Distribution Based on Severity Alcohol Dependence Syndrome.

9. Distribution Based on Severity Alcohol Withdrawal Syndrome

The distribution of alcohol withdrawal syndrome shows that patients 39 [33%] of the mild

withdrawal symptoms. About 40 patients [33%] of the patients experienced moderate withdrawal symptoms. 41 patients [34 %] of the patients had severe alcohol withdrawal symptoms, which is the highest proportion.

Table No. 30: Distribution Based on Severity Alcohol Withdrawal Syndrome.

Sl. No	Severity of AWS	No. of Patients	Percentage
1	Mild	39	33%
2	Moderate	40	33%
3	Severe	41	34%

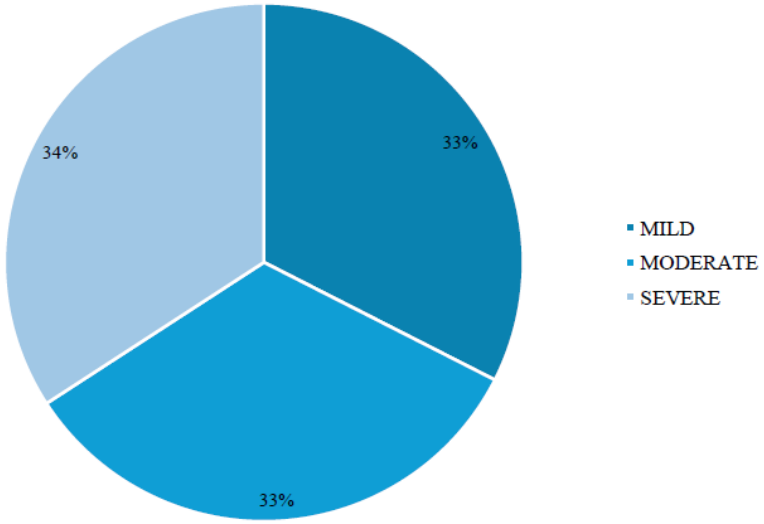

Figure no – 18 :- Distribution Based on Severity Alcohol Withdrawal Syndrome

10. Distribution Based on Severity of Sleep

According to sleep pattern distribution data shows that 1% had good sleep. About 19% of the patients experienced poor sleep. 38% of the patients had moderate sleep quality. The highest proportion, 42% of patients, suffered from severe sleep problems. This indicates that most patients had moderate to severe sleep disturbances.

Table No. 31: Distribution Based on Severity of Sleep abnormality.

Sl. No	Severity of Sleep	No. of Patients	Percentage
1	Good sleep	01	0.83%
2	Poor sleep	23	19.17%
3	Moderate sleep	46	38.33%
4	Severe sleep	50	41.67%

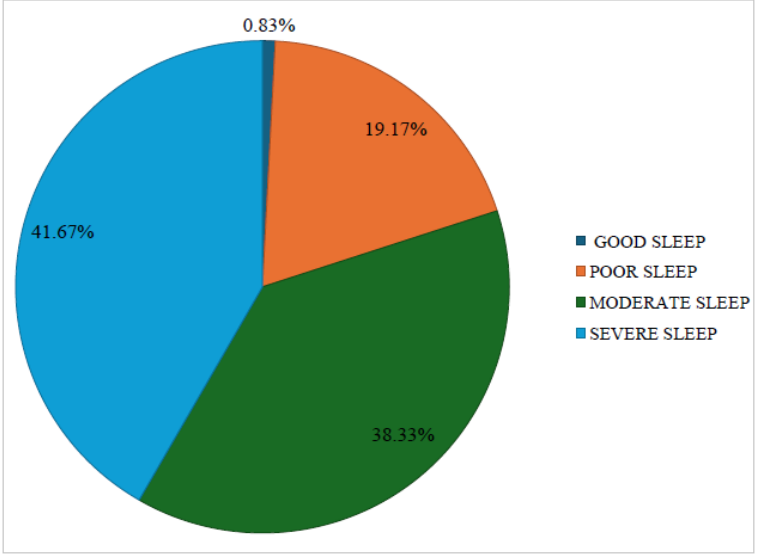

FIgure No. 19: Distribution Based on Severity of Sleep abnormality.

11. Distribution Based on Cognitive Function

According to cognitive function distribution data, among them 52 [43.3%] had mild cognitive impairment, 37 [30.85] had normal cognitive function , 29 [24.25] had moderate impairment, and only 2 [1.7%] had severe cognitive impairment.

Table No. 32: Distribution Based on Severity of Cognitive Impairment.

Sl. No	Severity of Cognition	No. of patients	Percentage
1	Normal	37	30.8%
2	Mild	52	43.3%
3	Moderate	29	24.2%
4	severe	02	1.7%

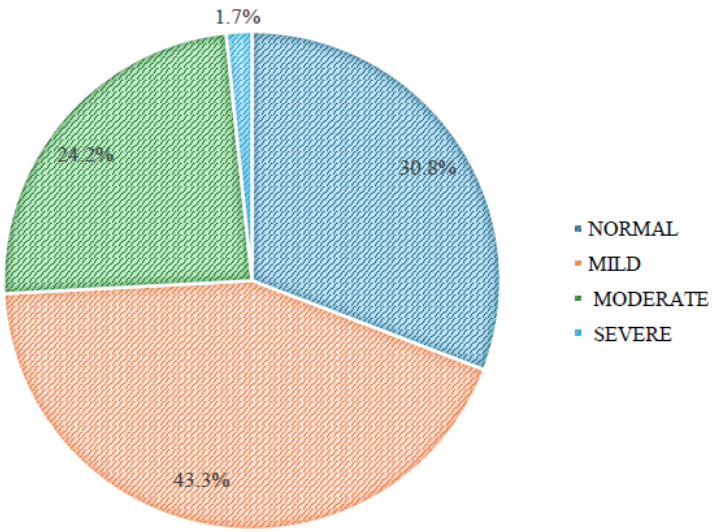

Figure No. 20: Distribution Based on Severity of Cognitive Impairment.

12. Distribution Based on Drugs used by Patients

Among 120 patients, 48 [40%] were treated only with Chlordiazepoxide, while 18 [15%] received only Lorazepam. 41 patients [34.2%] were changed from lorazepam to Chlordiazepoxide. Dose increase was observed in 1 patient [0.8%] for lorazepam and 7 patients [5.8%] for Chlordiazepoxide. Additionally, 5 patients [4.2%] were shifted from Chlordiazepoxide to Lorazepam.

Table No. 33: Distribution Based on Lorazepam Traits.

LORAZEPAM			
Trait→	**Only Lorazepam used**	**Lorazepam dose increased**	**Change Lorazepam to Chlordiazepoxide**
No. of Patients	18	01	41
%	15%	0.8%	34.2%

Table No. 34: Distribution Based on Chlordiazepoxide Traits.

CHLORDIAZEPOXIDE			
Trait→	**Only chlordiazepoxide used**	**Chlordiazepoxide dose increased**	**Change chlordiazepoxide to lorazepam**
No. of Patients	48	07	05
%	40%	5.8%	4.2%

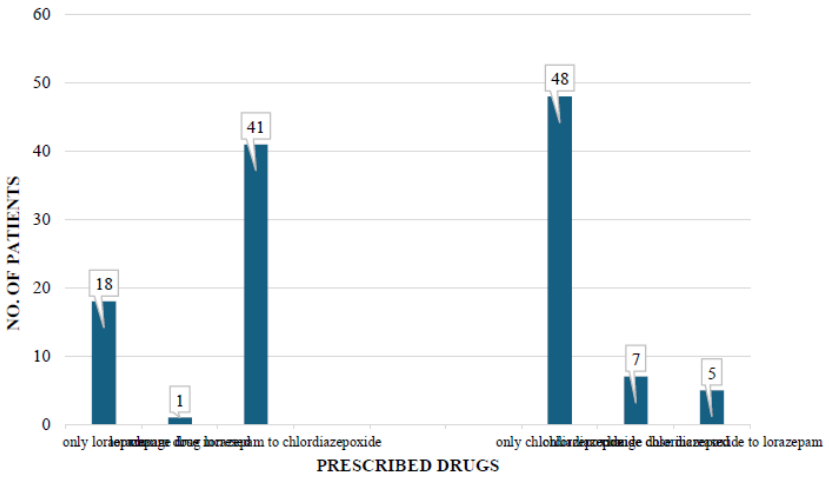

Figure No. 21: Distribution based on Lorazepam and Chlordiazepoxide Traits.

DISCUSSION

This Comparative Observational Study was conducted over six months in a Tertiary Care Hospital to assess the demographic, epidemiological and clinical profile of patients with alcohol – related diseases. The study population consisted of 120 patients who met the Inclusion criteria, allowing for a comprehensive analysis of various factors contributing to

alcohol – related illness.

The majority of patients are visited to Psychiatric Department (100%). The highlights of predominance of Alcohol related diseases in only Males, because Females are not consume much alcohol when compare to Males if consume they are not able to come Hospital to therapy due to some reasons.

Patients are predominantly in the 31 – 40 age range (56%), suggesting that prolonged alcohol consumption significantly develops Alcohol Dependence and Withdrawal Syndromes with Sleep and Cognitive Impairments. These age group followed by 41 – 50 age group (45%), 51 – 60 age group (12%), 20 – 30 age group (6%) and the lowest age group is 61 – 70 age group with 1 % only.

In 100 % Male patients upto 92.5% patients are Educated and Married who are addicted to alcohol when compare to Un – Educated and Un – Married patients and the percentage is 7.5 % only.

Duration of Alcohol intake is also evaluated, showing that 35% of the patients are consume alcohol between 11 – 15 years. While 8% are the patients who are consume alcohol from below 0 – 5 years.

Based on Quantity of Alcohol the distribution is evaluated, 40% of patients consume upto 180 – 360 ml of alcohol majorly followed by > 360 ml quantity of alcohol is consumed by 38%; while 21.7% patients are lowest quantity (90-180 ml) of alcohol consumers.

Based on the severity of Alcohol Dependence Syndrome the distribution is calculated as in 100%; only 20% patients are Mild, 54% patients are Moderate, 42% patients are Severe. Like in Alcohol Withdrawal Syndrome 33 % patients are Mild , 33% patients are Moderate, 41 % patients are Severe.

The another type of Distribution is based on Other Addiction such as Smoking, Tobacco Chewing in which 65.8% patients are severely addicted, 13.3% patients are Occasional addicted and 20.8 % are No addicted to any other substances.

On the other hand Sleep and Cognitive Impairment distribution is based on the Severity those categories are distributed. In Sleep impairment, patients who have Good Sleep is 0.83% and 41.67% patients are Severe Sleep while 19.17% are the patients who have Poor sleep and

with Moderate sleep is 38.33%.

In Cognitive Impairment, Patients who have Normal impairment is 30.8% and 1.7% have Severe impairment while 43.3 % and 24.39 % are Mild and Moderate Cognitive Impairment respectively.

The drugs distribution is also done based on the traits of Lorazepam and Chlordiazepoxide such as only the drug prescribed, increase the dose, change the drug from the therapy.

When come to Lorazepam upto 15 % of patients are taken only , for 0.8% Lorazepam dose is increased for potential action while upto 34.2% of patients therapy is changed to Chlordiazepoxide.
Unlike in Chlordiazepoxide upto 40 % of patients are taken only , for 5.8 % Chlordiazepoxide dose is increased for potential action while upto 4.2 % of patients therapy is changed to Lorazepam.

CONCLUSION

In conclusion, we have presented about The Comparative Observational Study provides comprehensive insights into demographic and clinical profile of patients with alcohol – related diseases. Alcohol Dependence Syndrome (ADS) and Alcohol Withdrawal Syndrome (AWS) is a significant chronic disorder that not only leads to physical disturbance on alcohol but also affects multiple aspects of mental health, particularly sleep quality and cognitive functioning**.** The present study evaluated 120 alcohol- dependent patients in the Psychiatric Department of APVVP Hospital, Proddatur**,** to assess the extent of sleep disturbances and cognitive impairment.

The findings of the study indicate that alcohol consumption was observed in 100% of male participants, highlighting the high prevalence of alcohol use among the male population in the study setting. A large proportion of patients were categorized under moderate and severe stages of Alcohol Dependence Syndrome, indicating a substantial level of alcohol-related health burden. Similarly, Alcohol Withdrawal Syndrome (AWS) was also commonly observed with varying degrees of severity among patients.

Sleep assessment results demonstrated that most patients experienced moderate to severe sleep abnormalities**,** while only a very small percentage of patients had good sleep quality. This suggests that chronic alcohol consumption significantly disrupts normal sleep patterns**,**

leading to poor sleep quality, reduced sleep duration, and fragmented sleep architecture.

Cognitive evaluation revealed that a majority of patients showed mild to moderate cognitive impairment**,** affecting functions such as memory, attention, and executive abilities. These impairments are likely associated with the neurotoxic effects of long-term alcohol exposure on the brain**,** which can interfere with daily functioning and negatively influence treatment outcomes.

In terms of pharmacological management, Benzodiazepines such as Chlordiazepoxide and Lorazepam were commonly used, with chlordiazepoxide being more frequently improve the signs and symptoms than Lorazepam for the management of alcohol induced diseases symptoms.

Overall, the study concludes that alcohol diseases is strongly associated with significant sleep disturbances and varying degrees of cognitive impairment. Early identification of these complications using standardized assessment tools is essential for effective clinical management, improved treatment outcomes, and relapse prevention**.** Comprehensive treatment approaches that include withdrawal management, psychological support, cognitive evaluation, and sleep management strategies are necessary to improve the overall quality of life in patients with Alcohol Dependence Syndrome.

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ANNEXURE – 1

SRI LAKSHMI VENKATESWARA INSTITUTE OF PHARMACEUTICAL SCIENCES

PRODDUTUR

INFORMED CONSENT FORM

Namaste My name is_____we are conducting a study on "**CLINICAL ASSESSEMENT OF SLEEP QUALITY AND COGNITION IN ALCOHOL DEPENDENCE AND WITHDRAWAL SYNDROMES – A COMPRATIVE TREATMENT STUDY**". We would very much appreciation the participation of you in this study participation in the study in voluntary and you can choose any question to answer. Whatever the information you provide will be kept confidential however we hope that you will participate in the study since your participation is important.

Signature of patient Signature of Investigator

సమాచార సమ్మతి పత్రము

నమస్తే నా పేరు _____ "మద్యం పై ఆధారపడటం మరియు ఉపసంహరణ లక్షణ సంపుటి ల లో నిద్ర నాణ్యత మరియు అభిగాహన యొక్క వైద్యసంబంధమైన మూల్యాంకనం - ఒక తులనాత్మక చికిత్స అధ్యయనం" పై మేం ఒక అధ్యయనాన్ని నిర్వహిస్తున్నాం. ఈ అధ్యయనంలో మీరు స్వచ్ఛందంగా పాల్గొనడాన్నిమేము ఎంతగానో ప్రశంసిస్తాము మరియు సమాధానం ఇవ్వడానికి మీరు ఏదైనా ప్రశ్నను ఎంచుకోవచ్చు. మీరు అందించే సమాచారం ఏమైనప్పటికీ గోప్యంగా ఉంచబడుతుంది. అయితే మీరుపాల్గొనడం ముఖ్యం కనుక అధ్యయనంలో మీరు పాల్గొంటారని మేం ఆశిస్తున్నాం.

రోగి యొక్క సంతకం పరిశోధకుని యొక్క సంతకం

ANNEXURE – 2

SRI LAKSHMI VENKATESWARA INSTITUTE OF PHARMACEUTICAL SCIENCES

PRODDATUR

PATIENT QUESTIONAIRE FORM

PATIENT INFORMATION DETAILS :-

1. **Date** :-_____/_____/_____
2. **Patient name** :-_____
3. **Age** :-_____
4. **Op No** :-_____
5. **Education** :-_____
6. **Occupation** :-_____
7. **Income** :-_____
8. **Duration of alcohol intake** :-_____
9. **Type of alcohol** :-_____
10. **Quantity** :-_____
11. **Last drink** :-_____
12. **Married status** :-_____
13. **Other addiction** :-_____
14. **Dependence / withdrawal** :-_____
15. **Sleep quality** :-_____
16. **Cognitive function** :-_____
17. **Chief complaints** :-_____
18. **Treatment** :-_____

SEVERITY OF ALCOHOL DEPENDENCE QUESTIONARY (SADQ)

During that period of heavy drinking

1. The day after drinking alcohol, I woke up feeling sweaty. ( )

0. Almost never **1.** sometimes **2.** often **3**. nearly always

2. The day after drinking alcohol, my hands shook first thing in the morning. ( )

0. Almost never **1.** sometimes **2**. often **3.** nearly always

3. The day after drinking alcohol, my whole body shook violently first thing in the morning. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

4. The day after drinking alcohol, I woke up absolutely drenched in sweat. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

5. The day after drinking alcohol, I dread waking up in the morning. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

6. The day after drinking alcohol, I was frightened of meeting people first thing in the morning ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

7. The day after drinking alcohol, I felt at the edge of despair when I awoke. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

8. The day after drinking alcohol, I felt very frightened when I awoke. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

9. The day after drinking alcohol, I liked to have an alcoholic drink in the morning. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

10. The day after drinking alcohol, I always gulped my first few alcoholic drinks down as quickly as possible. ( )

0. Almost never **1.** sometimes **2**. often **3.** nearly always

11. The day after drinking alcohol, I drank more alcohol to get rid of the shakes. ( )

0. Almost never **1.** sometimes **2**. often **3.** nearly always

12. The day after drinking alcohol, I had a very strong craving for a drink when I awoke. ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

13. I drank more than a quarter of bottle of spirit in a day (or 1 bottle of wine or 7 beers) ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

14. I drank more than half bottle of spirits per day (or 2 bottles of wine or 15 beers) ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

15. I drank more than 1 bottle of spirits per day(or 4 bottles of wine or 30 beers) ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

16. I drank more than 2 bottle of spirits per day (or 8 bottles of wine or 60 beers) ( )

0. Almost never **1.** sometimes **2.** often **3.** nearly always

Imagine the following situations:

1. You have been completely off drink for a few weeks

2. You then drink very heavily for two days

How would you feel the morning after those two days of drinking?

17. I would start to sweat. ( )

0. Not at all **1.** Slightly **2.** Moderately **3.** quite a lot

18. My hands would shake. ( )

0. Not at all

19. My body would shake. ( )

0. Not at all **1.** slightly **2.** Moderately **3.** quite a lot

20. I would be craving for a ( )

0. Not at all **1.** Slightly **2.** Moderately **3.** quite a lot

TOTAL _____

Interpretation _____

- Score <16 - Mild Alcohol Dependence
- Score 16-30 - Moderate Alcohol Dependence
- Score 30/>30 - Severe Alcohol Dependence

CLINICAL INSTITUTE WITHDRAWAL

ASSESSMENT OF ALCOHOL SCALE, REVISED (CIWA-Ar)

1. Nausea and vomiting	score	(0 to 7)	( )
2. Tremors	score	(0 to 7)	( )
3. Paroxysmal sweat	score	(0 to 7)	( )
4. Anxiety	score	(0 to 7)	( )
5. Agitation	score	(0 to 7)	( )
6. Tactile disturbances	score	(0 to 7)	( )
7. Auditory disturbances	score	(0 to 7)	( )
8. Visual disturbances	score	(0 to 7)	( )
9. Headache, fullness in head	score	(0 to 7)	( )

10. Orientation and clouding of sensorium score (0 to 7) ( )

TOTAL :- _____

Interpretation

- Score ≤ 10 - Mild Withdrawal (do not need additional medications)
- Score 10-15 - Moderate Withdrawal
- Score ≥15 - Severe Withdrawal

PITTSBURGH SLEEP QUALITY INDEX

1. When have you usually gone to bed in the night?( )

0. 9 pm **1**. 9-11 pm **2.** 11-12 pm **3.** >12 pm

2. How long (in min)as to taken you to fall asleep each night? ( )

0. <15mins **1.** 16-30mins **2.** 31-60 mins **3.** >60 mins

3. When have you usually gotten up in the morning? ( )

0. 6am **1.** 6-8am **2.** 8-10am **3.** after 10 am

4. How many hours of actual sleep do you get at night ?{ This may be different than the number of hours you spend in the bed} ( )

0. >7=0 **1.** 6-7=1 **2.** 5-6=2 **3.** <5=3

5. During the past month, how often have you had trouble sleeping because you? ( )

0. 0 **1**. 1-5 times **2.** 6-12 times **3.** more than 12 times

a. Cannot get to sleep within 30 minutes
b. Wake up in the middle of the night or early morning
c. Have you get up to use bathroom
d. Cough or snore loudly
e. Feel too cold
f. Feel too hot
g. Have bad dreams
h. Have

TOTAL =

0. 0 **1.** 1-9 **2.** 10-18 **3.** 19-27

6. During the past month, how often have you taken medicine (prescribed or over) the counter) to help you sleep? ( )

0. 0 **1**. <4 **2.** 5-8 **3**. >8

7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activities ? ( )

10. 0 **1.** <4 **2.** 5-8 **3.** >8

8. During the past month, how much of a problem as it been for you to keep up enthusiasm to get things done ? ( )

0. 0 **1.** <4 **2.** 5-8 **3.** >8

9. During the past month,how would you rate your sleep quality overall? ( )

0. Very good **1.** fairly good **2.** fairly bad **3.** very bad

TOTAL :- _____

Interpretation

- Good sleep- Score - 0-4
- Poor sleep quality - Score - 5-9
- Moderate sleep disturbance - Score - 10-14
- Severe - Score - 14-18

MINIMENTAL STATE EXAMINATION

Orientation:-

1. What is the (year, season, date, day, month) ? Score 5 (/5)

2. Where are we (state, country, town, hospital, flour)? Score 5 (/5)

Registration

1. Name three objects: one second to say each. Then ask The patient all 3 after you have said them. Give one point for each correct answer, then repeat them until he/she learns all 3, count trails and recall. Score 3 (/3)

Attention and calculation

1. Serial 7s, 1 point for each correct answer, stop after 5 answers. Score 5 (/5)
Alternatively spell “word” backward.

Recall

1. Ask for the three objects repeated above. give one point for each correct answer. score 3 (/3)

Language

1. Name a pencil and watch. Score 2 (/2)

2. Repeated the allowing "no, ifs, ands, or buts'. Score 1 (/1)

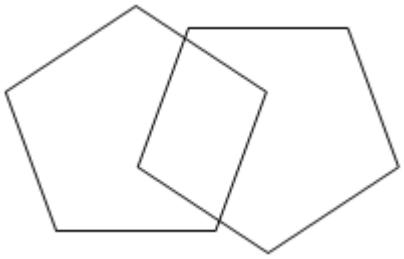
3. Follow a three stage command Score 3 (/3)

"a paper in your hand, fold it in half, and put it on the floor."

4. Read and obey the following "close your eyes." Score 1 (/1)

5. Write a sentence ? Score 1 (/1)

6. Copy the design shown Score 1 (/1)



TOTAL :- _____

Interpretation :-

- Normal cognition - Score - 24-30
- Mild cognitive impairment - Score - 18-23
- Moderate cognitive impairment - Score - 10-17
- Severe cognitive impairment - Score - <10

SUMMARY OF THE ANNEXURE (BEFORE ANY FOLLOW UP's)

Date:- _____ /_____20_____

Patient name : _____ Age_____ (years) OP.No_____

1. Patient diagnosed with ☐ Dependence ☐ Withdrawal ☐Both

Dependence

☐ Mild ☐Moderate ☐ Severe

Withdrawal :-

☐ Mild ☐Moderate ☐ Severe

SCALE SCORE

a. SADQ ☐ Mild ☐Moderate ☐ Severe

b. CIWA ☐ Mild ☐Moderate ☐ Severe

c. PSQI ☐ Mild ☐Moderate ☐ Severe

d. MMSC ☐ Mild ☐Moderate ☐ Severe

2. Drug Prescribed :- ☐Lorazepam ☐Chlordiazepoxide

3. Drug chart :-

Table No. 35. Drug chart for patient before follow up.

Sl.NO	Drugs Prescribed	Dose	ROA	Freq	Duration
1			ORAL		
2			ORAL		
3			ORAL		
4			ORAL		
5			ORAL		

PATIENT FOLLOW UP DATA

Follow up Date :- / /20

1. Signs and Symptoms ☐Reduced ☐Not reduced

If Not reduced Why ?

_____

_____

_____

2. Switch therapy to another drug ☐Yes ☐No ☐↑ Dose

If yes:- ☐Lorazepam ☐Chlordiazepoxide

If assess Switch Therapy to the patient the drug chart will be :-

Table No. 36: Drug chart for patient after follow up.

Sl.NO	Drugs Prescribed	Dose	ROA	Freq	Duration
1			ORAL		
2			ORAL		
3			ORAL		

4			ORAL		
5			ORAL		

PATIENT RE – FOLLOW UP DATA

Patient Re – follow up date :- / /20

1. Signs and Symptoms ☐Reduced ☐Not reduced If Not reduced Why ?

_____

_____

_____

2. Further Investigation :-

ANNEXURE – 3

SRI LAKSHMI VENKATESWARA

INSTITUTE OF PHARMACEUTICAL SCIENCES

PRODDATUR

PATIENT INFORMATION LEAFLET

Alcohol

Alcohol (ethanol) is a **psychoactive substance** found in beverages such as beer, wine, and spirits. It affects the **central nervous system (brain and spinal cord)** and changes mood, behavior, and thinking.

- **After drinking alcohol**

✓ It is quickly absorbed from the **stomach and small intestine**

✓ It enters the **bloodstream**

✓ It travels to the **brain, liver, heart, and other organs**

✓ The **liver breaks down alcohol**, but excessive intake can damage the liver and other organs.

- **SIGNS AND SYMPTOMS OF ALCOHOL**

▪ **Short-term effects of alcohol**

- ✓ Feeling relaxed
- ✓ Reduced anxiety
- ✓ Slurred speech
- ✓ Poor coordination
- ✓ Heart problems such as High Blood Pressure, Cardiomyopathy, Stroke
- ✓ Brain and nervous system effects such as Memory loss, Cognitive impairment, Peripheral Neuropathy
- ✓ Other health problems such as Gastritis,Ulcers, Pancreatitis, Weakened immune system, Increased cancer risk

Alcohol Dependence Syndrome

(ADS)

Alcohol Dependence Syndrome is a **chronic condition in which a person becomes dependent on alcohol both physically and psychologically**.

People with alcohol dependence feel a **strong urge to drink and find it difficult to stop**.

➢ Common Symptoms

- Craving
- Loss of control
- Tolerance
- Withdrawal symptoms
- Neglect of responsibilities
- Continued drinking despite harm

Alcohol Withdrawal Syndrome (AWS)

Alcohol Withdrawal Syndrome occurs when a person who has been drinking heavily for a long time **suddenly stops or reduces alcohol intake**.

The brain becomes **overactive** because it is used to the depressant effects of alcohol.

➢ Timeline of Withdrawal Symptoms

- **6–12 hours after last drink**

✓ Tremors

✓ Anxiety

✓ Headache

- ✓ Nausea
- ✓ Sweating
- ✓ Insomnia

- **12–24 hours**
- ✓ Hallucinations
- ✓ Increased blood pressure
- ✓ Irritability

- **24–48 hours**
- ✓ Seizures may occur
- **48–72 hours**
- ✓ Delirium Tremens (severe confusion, fever, hallucinations)
- Severe symptoms:
- ✓ Seizures
- ✓ Hallucinations
- ✓ Delirium tremens

Alcohol Induce Sleep Impairment

Alcohol can disturb **normal sleep cycles**. Although alcohol may make a person feel sleepy, it **reduces the quality of sleep**.

- ➢ Effects on Sleep
- ✓ Frequent waking during the night
- ✓ Reduced REM sleep
- ✓ Nightmares
- ✓ Snoring and sleep apnea
- ✓ Daytime sleepiness
- ✓ Long-term alcohol use can lead to **chronic insomnia**.

Alcohol Induce Cognitive Impairment

Long-term alcohol use can damage brain cells and lead to **problems with thinking, memory, and learning**.

- ➢ Symptoms of Cognitive Impairment
- ✓ Memory loss

- ✓ Difficulty concentrating
- ✓ Poor judgment
- ✓ Slowed thinking
- ✓ Difficulty learning new information

Alcohol-Related Brain Disorders

1. **Wernicke's Encephalopathy** Caused by vitamin B1 (thiamine) deficiency
2. **Korsakoff Syndrome** ; Severe memory disorder
3. **Alcohol-related dementia** ; Early treatment and stopping alcohol may improve brain function.

Lorazepam

Lorazepam belongs to the **benzodiazepine (BZD) group of medicines**.

- ➢ It is commonly used to treat:
- ✓ Alcohol withdrawal
- ✓ Anxiety
- ✓ Insomnia
- ✓ Seizures

- ➢ Usual Dose

Dose depends on severity and doctor's judgment.

Typical doses include:

- **Mild withdrawal** :- 1–2 mg orally every 6–8 hours
- **Moderate withdrawal** :- 2–4 mg orally every 6 hours
- **Severe withdrawal**:- 2–4 mg intravenously every 15–30 minutes until symptoms are controlled
- Maximum dose varies depending on patient response.

- ➢ Advantages

- Safe in liver disease
- Rapid onset of action
- Effective in controlling seizures

➢ Side Effects

- Drowsiness
- Dizziness
- Confusion
- Weakness
- Poor coordination

➢ Safety Advice

- Take only as prescribed
- Avoid alcohol
- Do not drive if feeling sleepy
- Do not stop suddenly without medical advice

Chlordiazepoxide

Chlordiazepoxide is also a **benzodiazepine** and is widely used in **alcohol withdrawal treatment**.

➢ **Usual Dose**

Typical dosing schedules

- **Initial dose**:- 25–50 mg orally every 6 hours
- **Moderate withdrawal**:- 50– 100 mg every 4–6 hours
- **Severe withdrawal**:- Up to 300 mg per day in divided doses
- Thedose is gradually **reduced over 3–7 days.**

➢ **Advantages**

- Long duration of action
- Smooth withdrawal control
- Prevents seizures and delirium tremens

➢ **Side Effects**

- Sleepiness
- Dizziness
- Dry mouth
- Poor coordination
- Confusion (especially in elderly)

Safety Advice for Lorazepam & Chlordiazepoxide

- Take only under medical supervision
- Avoid alcohol during treatment
- Follow the prescribed dosage schedule

Prevention of Alcohol Dependence and Withdrawal Syndromes

Preventing alcohol-related diseases is very important.

1. Limit Alcohol Consumption

- Follow recommended drinking limits
- Avoid binge drinking

3. Avoid Drinking to Cope with Stress

Instead of alcohol do

- Exercise
- Meditation
- Talk to friends or family
- Seek counseling

3. Maintain Healthy Lifestyle

- Eat balanced meals
- Get enough sleep
- Stay physically active

6. Support Groups

Groups such as **Alcoholics Anonymous (AA)** provide support for recovery.

7. Family Support

Family encouragement and emotional support play an important role in recovery.

4. Attend follow-up visits

5. Avoid triggers that lead to drinking

6. Seek counseling or rehabilitation if needed

When to Seek Immediate Medical Help

Contact a doctor or visit the hospital immediately if the patient develops:

- Seizures
- Severe confusion

- Hallucinations
- High fever
- Severe agitation
- Loss of consciousness

4. Education and Awareness

- Understanding the risks of alcohol helps prevent addiction.

5. Early Medical Help

If someone shows early signs of alcohol dependence:

- Seek medical advice
- Attend counseling or therapy General Advice for Patients

1. Do not suddenly stop heavy alcohol consumption without medical supervision
2. Follow doctor's instructions carefully
3. Take prescribed medications regularly