

**PSYCHIATRIC COMORBIDITY IN PATIENTS WITH OPIOID DEPENDENCE**

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**ABSTRACT****BACKGROUND**

Opioid dependence is a major public health problem in Kerala. Presence of psychiatric disorder among opioid dependent patients worsens the scenario. To date no attempts have been made to analyse the magnitude and pattern of comorbid psychiatric disorders in the state.

**MATERIALS AND METHODS**

We assessed 30 patients with ICD-10 diagnosis of opioid dependence syndrome for the presence of comorbid psychiatric disorders using structured clinical interview for DSM IV Axis 1 disorder (SCID-1). Patients with opioid withdrawal state, delirium and acute medical emergencies were excluded.

**RESULTS**

56.7% of our subjects had a comorbid psychiatric disorder. Major depressive disorder was the most common one (n=7, 23.3%). Prevalence of other disorders were generalised anxiety disorder (n=6, 20%), bipolar affective disorder (n=3, 10%) and schizophrenia (n=1, 3.3%).

**CONCLUSION**

Comorbid Psychiatric disorders are highly prevalent in opioid dependence. There is a need for further large sample studies in the areas of comorbidities and in the integrated strategies for the identification and management of both opioid dependence and comorbid psychiatric disorders.

**KEYWORDS**

Opioid Dependence, Comorbidity, Psychiatric Disorders.

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**BACKGROUND**

Opioids include substances such as morphine, heroin, codeine, oxycodone, hydrocodone, pentazocine, propoxyphene etc. Opioid dependence is characterized by the development of tolerance (increased use overtime), craving (irresistible urge to use and procure opioids) and withdrawal syndrome when opioid use is stopped and continued use of opioids in spite of adverse consequences.

According to UNDCP report, the prevalence rate of opiate user is 0.4% for India. Considering the total population of India, the number of users will be around an

alarming estimate of 50 Lakhs. It is reported that many of opioid dependent patients also are reported to be sufferers of illnesses like HIV, Hepatitis B and C.<sup>1</sup> Opioid use disorders are progressively increasing cause of deaths too. Opioid use disorders resulted in 51,000 deaths worldwide in 2013 where as it was estimated to be 18,000 deaths in 1990.

Psychiatric comorbidities are of importance in opioid dependence due to various reasons. Presence of psychiatric disorders may be 1) A risk factor developing opioid dependence; 2) May influence the treatment outcome of opioid use disorder, functionality, suicidality; and 3) Some studies shows that patients with opioid dependence are more prone to develop dependence to treatment of anxiety disorders (like benzodiazepines). So, identification and proper treatment of psychiatric disorders are important in opioid dependence.

Comorbidity varies across studies. Rounsaville et al<sup>2</sup> reported that 80% of opioid abusers had comorbid psychiatry diagnosis. However, some other studies reported lower prevalence rates ranging between 47-49%<sup>3</sup> of comorbid psychiatric diagnosis. Kaplan and Saddock<sup>4</sup> found

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that about 90% of persons with opioid dependence have comorbid psychiatric disorders. Variation in figures of co-existing psychiatric disorders is understandable in view of the widely different diagnostic criteria used, the different populations studied and different settings.

The most common diagnoses were major depressive disorder and anxiety disorder. A study by Lintzeris et al<sup>5</sup> revealed that compared with general population, the opioid dependent individuals tend to have 7 times greater incidence of a psychotic disorder, 9 times greater incidence of a diagnosis of depression and 3 times greater incidence of a diagnosis of anxiety. Life-time prevalence of mood depression in subjects with opioid dependence is higher than in the general population (44-54% versus 16%)<sup>6</sup> and represents a risk factor for morbidity and mortality, with a relevant increased risk for completed suicide.<sup>7</sup> Opioid dependent persons are especially at risk for the development of brief depressive symptoms, and for episodes of mild to moderate depression that meet symptomatic and duration criteria for major depressive disorder or dysthymia. These syndromes represent both substance-induced mood disorders as well as independent depressive illnesses. Suicide is a well-known cause of mortality causes among opiate abusers, and suicide attempts in opiate dependence is 13.5 times more common than in general population.<sup>7,8</sup>

Another common psychiatric disorder in persons with opioid dependence is antisocial personality disorder. Studies have found rates of antisocial personality disorder ranging from 20 to 50% in opioid dependence compared to less than 5% in the general population. Insomnia is common, especially during withdrawal; sexual dysfunction, especially impotence, is common during intoxication. Delirium or brief, psychotic - like symptoms are also seen during opioid intoxication. Less than 5% of persons with opioid dependence have psychotic disorders such as bipolar illness or schizophrenia. Substance use disorders like alcohol and cannabis is also very common in opioid dependence than in general population.<sup>3</sup>

The data on psychiatric comorbidity among opioid addicts and its negative effect on outcome<sup>9</sup> have stimulated research on the effect of combining psychiatric and substance abuse treatment. Studies have shown that tricyclic antidepressants can be useful for chronically depressed opioid dependent persons who are treated with methadone maintenance. Two other studies have shown that psychotherapy is useful in opioid dependence comorbid with psychiatric disorder (Woody et al, 1999). The main result in most pharmacotherapy and psychotherapy studies with methadone-maintained addicts has usually been a reduction in psychiatric symptoms such as depression.<sup>10</sup> A few studies have shown that the intervention for coexisting psychiatric morbidity may improve the outcome of opioid substitution therapy and that presence of comorbid depression to have negative outcome on treatment of opioid addiction.<sup>3,8,11</sup>

In prescribing medications for comorbid non-substance related psychiatric disorders, psychiatrists should be aware to the dangers of medications with high abuse potential (eg.

benzodiazepines) and to possible drug interactions between opioids and other psychoactive substances.<sup>10,12</sup> In general, benzodiazepines having a rapid onset, such as diazepam and alprazolam should be avoided in treating anxiety disorders because of their very high abuse potential in opioid dependence.<sup>13</sup>

Comorbid opioid dependence and psychiatric disorders require special attention, since treatment directed at opioid dependence alone is unlikely to be beneficial because, depressive symptoms or anxiety disorders may again prompt abstinent patients to resort to opioids to get rid of such mood states (as opioids have mood elevating and anxiolytic properties).

Currently the focus of treatment for opioid dependence is harm reduction, to reduce the usage and to reduce the harm of injectable opioids. The most common treatment strategy employed is opioid substitution therapy (OST) with oral methadone or buprenorphine. The only agent for opioid substitution therapy in India is buprenorphine. Buprenorphine is related to morphine; it is a partial agonist that functions on the same brain receptors as morphine, but does not produce the same high, dependence or withdrawal syndrome. It is long-lasting, less likely than morphine (or other full receptor agonists) to cause respiratory depression and is well-tolerated by patients. OST units functions across India and they provide diagnostic services, substitution therapy, counseling services and it is a directly observed treatment programme, i.e. patients should attend the clinic/ centre at prescribed time to get their medication. It provides direct supervision, dose titration and ensures abstinence from injectable opioids by clients. It is an excellent opportunity for the treating team to detect psychiatric disturbances earlier and to treat by pharmacological and psychotherapeutic approaches and to follow up them more closely.

### **Rationale of the Present Study**

Though well described in western literature, the prevalence and pattern of psychiatric disorders in opioid dependence is not systematically studied in India. Evaluating patients with opioid dependence for psychiatric disorders is important to maintain abstinence and prevent relapses. So we aimed to study psychiatric comorbidity in patients with opioid dependence using well validated structured interview schedule.

Our study aimed to find the prevalence of psychiatric comorbidities among patients with opioid dependence attending psychiatry outpatient department and opioid substitution therapy (OST) unit of Govt. medical college, Manjeri.

### **MATERIALS AND METHODS**

**Study Design-**Cross-sectional observational study.

**Study Subjects-** The study sample will consist of about 30 patients with opioid dependence attending psychiatry outpatient department and opioid substitution therapy (OST) unit of Govt. Medical College, Manjeri. (30 is the

average number of opioid dependence patients attending these two facilities over 3-4 months).

**Study Period-** May 2016 to August 2016.

**Inclusion Criteria-** Adults aged between 18-60 years.

**Exclusion Criteria-** Opioid withdrawal state, Delirium, Acute medical emergencies.

**Tools Used**

1. Clinical data sheet (of factors related to onset of opioid use, dose, social/legal/physical/psychological problems of opioid use, OST treatment details) & Sociodemographic data sheet (to collect age, gender, employment, education and residential status).
2. Structured clinical interview for DSM-IV Axis I disorders (SCID-I) – It is a structured interview to evaluate for psychiatric disorders.
3. Clinical opiate withdrawal scale (COWS).
4. Hamilton depression rating scale (HAM-D).
5. Hamilton Anxiety Rating Scale (HAM-A).

**Procedure**

All patients with opioid dependence attending the above-mentioned facilities will be screened for exclusion and inclusion criteria. Consented patients will be assessed using the tools mentioned.

**Statistical Analysis**

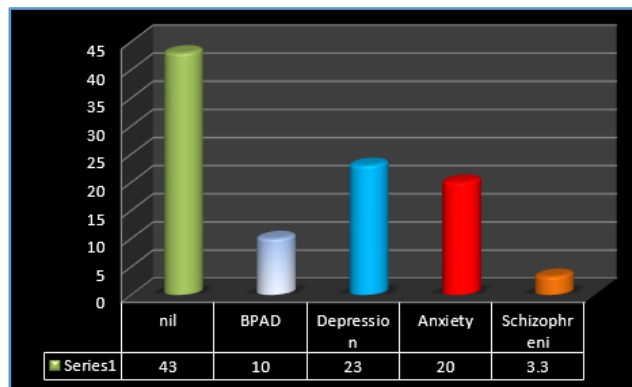
Statistical Package for Social Sciences (SPSS) will be used for data analysis. The prevalence of various psychiatric disorders will be expressed in frequency - n (%).

**RESULTS**

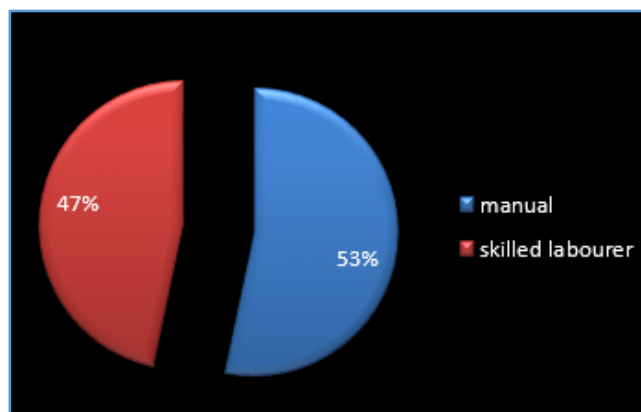
A total of 30 patients were included. All the participants were male. Majority were in the age group of 50-60 years (n=10, 33.3%), married (n=27, 90%), had completed tenth standard education (n=4, 13.3%), manual labourers (n=16, 53.3%), skilled workers (n=14, 46.7%), and earning in the range of 25000-35000 INR per month (n=16, 53.3%). Age of initiation was between 11-20 years in (n=22, 73.3%) and 21-30 years in 8(26.7%) subjects, while the duration of opioid dependence was in 16-20-year range in 12 (40%) of them. Maximum mode of use was inhalation and intravenous injections (n=12, 40%). Other substances used along with opioids were tobacco (n=14, 46.7%), Ganja (n=10, 33.3%), tobacco, ganja and alcohol together (n=5, 16.7%). 56.7% of our subjects had comorbid psychiatric disorders. Major depressive disorder was the most common one (n=7, 23.3%). Prevalence of other disorders were Generalised Anxiety Disorder (n=6, 20%), Bipolar affective disorder (n=3, 10%) and Schizophrenia (n=1, 3.3%). Most of the patients started opioid use due to peer pressure (n=21, 70%). Majority of the subjects were aware of the hazards of opioid use and its complications. There was no statistical significance between years of dependence and major psychiatric illness (p=0.561).

**DISCUSSION**

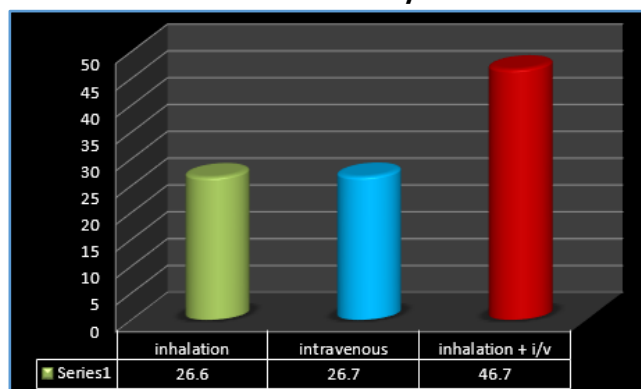
Our sample contained relatively elderly patients (mean age 43.6 years, SD 12.13) and age of onset of opioid use was relatively early (mean 19.9 years, SD 3.898). The mean duration of dependence was 15.3 (SD 6.25) years. All our study subjects were males. The prevalence of opioid use among women is substantially low as it is not culturally acceptable. Psychiatric comorbidity was found in 56.7% of our subjects. This is comparable to the findings of Brooner et al study (47-49%).<sup>3</sup> This further illustrates the heterogeneity of the patients of psychoactive substance dependence and implies that it should coax the clinician not to stop with a single diagnosis.



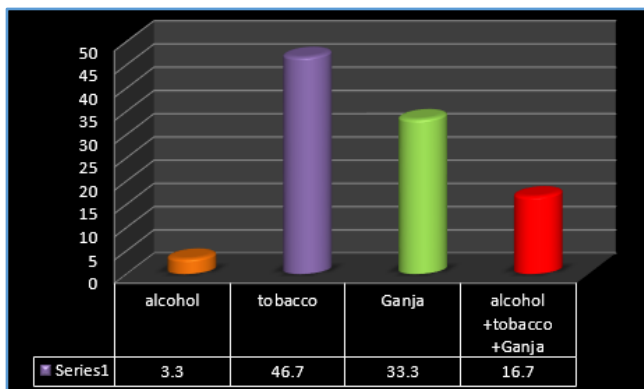
**Figure 1. Bar Diagram showing the Percentage of Various Psychiatric Comorbidities**



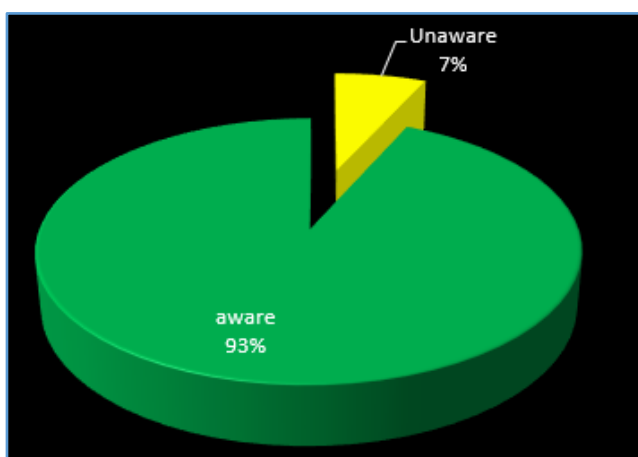
**Figure 2. Pie Diagram showing the Percentage of Distribution of Occupation**



**Figure 3. Bar Diagram showing the Percentage of Distribution of Mode of Use**



**Figure 4. Bar Diagram showing the Percentage of Distribution of Use of Other Substance**



**Figure 5. Pie Diagram Showing the Percentage of Distribution of Awareness**

Psychiatric comorbidity was found in 56.7% of our subjects. This is comparable to the findings of other studies. For example, Brooner et al<sup>3</sup> reported psychiatric comorbidity of 37%, 47% respectively. Similar by Rounsaville et al<sup>2</sup> reported that 39% patients had an additional psychiatric diagnosis. However, Kessler et al<sup>14</sup> reported about 50%, Darke et al<sup>8</sup> 60% and Limbeek et al<sup>15</sup> reported 85% additional psychiatric co-morbidity in their opioid dependent population. On the contrary Merikangas et al<sup>16</sup> reported less than 10% psychiatric co-morbidity in their samples. As discussed earlier there can be several reasons for these wide variations, including widely different population studied by different authors, the context (whether the study is conducted in outpatients, inpatients or community sample), the tools used (whether a structured interview schedule was used to diagnose comorbidities or not) and stage of illness (whether the evaluation was done during active use or remission). The relatively higher psychiatric morbidity in our sample can be attributed to a number of variables. One of the reasons seem to be, that the duration of drug dependence in this population was quite long, on an average about 16 years in about 40% of the study subject. It appears that psychiatric co-morbidity tends to accumulate with time probably due to the effects of the drugs on central nervous system and the resulting social and psychological complications.

Depression was the most commonly associated co-morbid condition. Around 23% patients had major depression. This is consistent with the findings of Limbeek et al<sup>15</sup> and Regier et al<sup>17</sup> while Rounsaville et al<sup>2</sup> reported a high figure of around 48% with major depression in their samples. Although Musharaf and Rehman reported a much lower figure of less than 2% in their study. It has to be noted that this was a retrospective study based on case notes which could have inherent problems. The findings of this study along with those of other studies, indicate that about one third of patients suffering from opioid dependence have additional depressive illness. These findings seem to lend support to the hypothesis of a relatively high prevalence of psychiatric co-morbidity among opioid dependents seeking treatment.

In this population a lower prevalence of anxiety disorders, psychotic illnesses including mania and schizophrenia were found. Generally, anxiety and the psychotic disorder have been found to be less associated with opioid dependence. GAD was diagnosed in 20%, and this prevalence is similar to the findings by Kushner et al<sup>18</sup> However comorbidity of schizophrenia and substance abuse has attracted considerable attention in recent years as the comorbidity of the two conditions is rapidly increasing, Fowler et al. reported a higher prevalence of about 26% for overall substance abuse in schizophrenia however opioid has been reported in 2-9% only. Similarly, Cantwell et al<sup>19</sup> showed that 7% of sample of 1st episode psychosis met the diagnosis of substance abuse including 8.4% with substance related psychotic disorder. There is agreement amongst most authors that substance abuse and schizophrenia are associated not only with violence but also with a number of other problems including poor treatment adherence, an increased suicide risk, increased rates of hospital admission and HIV infections.

**Limitations**

Limitations of our study include small sample size, cross-sectional design and including only outpatients. We did not assess physical comorbidity or treatment parameters. Personality evaluation scales or structured interview schedule for axis II disorders could have been used to detect personality disorders. Population of the study from a tertiary care center may not be truly representative of opioids dependent in general and there was no control group to compare the psychiatric co-morbidity.

**CONCLUSION**

Psychiatric comorbidities are very common in opioid dependence. It is evident that the sample had significant psychiatric comorbidity. Most common psychiatric disorder is major depression. In clinical practice most of these disorders go undetected even in the tertiary care centers. Psychiatric disorders are associated with poor treatment response to opioid substitution therapy and increased rates of suicide. Identification and treatment of comorbid disorders like depression will improve abstinence rates and reduce relapses. Detection and treatment of depression has

significant primary and secondary preventive role in the management of substance dependence. So there is a need for screening all opioid dependents for psychiatric disorders who come for detoxification. Only a few studies have evaluated the prevalence of psychiatric disorders in opioid users in India. Studies with larger sample size, studies that include patients with remitted opioid use, and studies on integrated interventions to treat both opioid and the comorbid psychiatric disorders are needed in the future.

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