



“A COMPARATIVE STUDY OF ANXIETY AND DEPRESSION BETWEEN INTRAVENOUS DRUG ABUSERS AND NON-INTRAVENOUS DRUG ABUSERS ATTENDING DEPARTMENT OF A TERTIARY CARE HOSPITAL OF NORTH EAST INDIA”

Psychiatry

Dr. Niladri Debbarma

Consultant Psychiatrist, Gomati District Hospital, Tapania, Gomati Tripura, India

Dr Kamal Das

Assistant Professor, Department Of Dermatology, AGMC & GBP Hospital, Tripura, India

Dr. Priyajyoti Chakma*

Assistant Professor, Department Of Psychiatry, AGMC & GBP Hospital, Tripura, India
*Corresponding Author

Dr Chaitali Malakar

Senior Resident, Department Of Psychiatry, AGMC & GBP Hospital, Tripura, India

Dr Munmun Debbarma

Senior Resident, Department Of Psychiatry, AGMC & GBP Hospital, Tripura, India

Dr Aparajita Pal

Assistant Professor, Department Of Obs & Gynae, AGMC & GBP Hospital

ABSTRACT

Background: Globally the number of opioid abusers are increasing day by day & overall, in the country, the prevalence of current use of any opioid is 2.06%. Heroin is the most commonly used opioid in India (1.14%). This was followed by pharmaceutical opioids (0.96%) and opium (0.52%). But unlike the European and American countries, the use of heroin through injection route has not been one of the popular routes in most parts of India, except the North Eastern states. People who use drugs are particularly susceptible to mental health disorders, the most common being mood and anxiety disorders, suicidal ideation, and suicide attempt. This study, therefore, is an attempt to estimate the proportion and compare anxiety and depression among intravenous opioid abusers and non-intravenous opioid abusers. **Methods:** ICD-10 Diagnostic Criteria was used for diagnosis of Anxiety & Depression of the study subjects. Sociodemographic information was gathered as per prepared standard questionnaire. Hamilton Anxiety Rating Scale (HAM-A) & Hamilton Depression Rating Scale (HAM-D) was used to assess the severity of the Anxiety & Depression among the 140 study subjects. **Result:** This study had shown that opioid abuse is higher among 21 to 25 years of age group among intravenous users whereas non intravenous route of intake was more common among 25-30 years age group. 60% of the participants reported opioid intake by intravenous route while 40% reported non intravenous route of intake. 18 (21.4%) patients of intravenous users were having mild anxiety and 8 (9.5%) patients had moderate anxiety. Whereas 11 (19.6%) patients of non-intravenous users, had mild anxiety and 7 (12.5%) patients had moderate anxiety. In the intravenous group, 17 (20.2%) patients had mild depressive symptoms, 12 (14.3%) patients had moderate and 13 (15.5%) patients had severe depressive symptoms. In non-intravenous group, 17 (30.4%) patients had moderate depression. This was statistically significant ($p < 0.0001$). **Conclusion:** There is scanty data available on the prevalence of psychiatric morbidities among opioid abusers & their severity in the states of North-Eastern India, particularly Tripura. Clinicians should routinely assess for anxiety and depression in patients with opioids abuse disorders which tend to go undiagnosed and in turn increase substance taking behaviour. Our study shows the need of further researches on this topic for a better understanding to detect psychiatric morbidities among drug abusers at the earliest, so that appropriate treatment can be initiated at the earliest and benefit to the patient can be maximized.

KEYWORDS

Drug Users, Opioid, Depression, Anxiety

INTRODUCTION:

Globally the number of opioid abusers are increasing, we realize that opioid abusers are increasing in Tripura too, and these people are prone to develop a number of psychiatric comorbidities.

Overall, in the country, the prevalence of current use of any opioid is 2.06%. Heroin is the most commonly used opioid in India (1.14%). This was followed by pharmaceutical opioids (0.96%) and opium (0.52%). [1] But unlike the European and American countries, the use of heroin through injection route has not been one of the popular routes in most parts of India, except the North Eastern states. [2]

The frequency of anxiety and depression is elevated among individuals with opioid abuse and these disorders are associated with continued substance use despite treatment and causes harm to the well-being of the individual and affects the family as well. Most of the time it is reported as underdiagnosed and a majority of patients go untreated. Many studies have indicated that comorbid depressive symptoms play a major role in the prognosis of substance use disorder and the relapse has been found to be greater in patients who have a comorbid depression.

Injection drug users (IDUs) are also highly vulnerable to contract HbsAg, HCV and HIV infection. Physical, psychological and social dysfunctions resulting from drug addiction can add to the stress of living, accelerating the deterioration of mental health.

People who use drugs are particularly susceptible to mental health disorders, the most common being mood and anxiety disorders,

suicidal ideation, and suicide attempt. Among people who inject drugs (PWID), the prevalence of mental disorders can reach 40% and increases significantly if the individual has a lifetime prevalence of mental disorders. [3]

Determinants of psychiatric disorders among PWID may include social, environmental, psychological and medical factors and may differ based on the type of substance used. HIV/HCV seropositivity, gender, mostly female, trauma during childhood, stigma due to drug use and excessive alcohol use are commonly associated with depression. Drug users suffering from mental health disorders are more likely to engage in high-risk behaviors and have negative outcomes for the treatment of HIV infection and substance use disorders. [4, 5]

HIV infection is common among PWID, and people suffering from mental health disorders may delay access to antiretroviral treatment (ART). They also tend to have poor virologic response to first-line ART, have low adherence to treatment, impaired quality of life, and may exhibit increased prevalence of sexual related risk behaviors. [6]

Haiphong, the largest harbor city in North Vietnam inhabits a population of 5,000 PWID [7] with 3,955 patients treated with methadone in March 2017 (Vietnamese Ministry of Health). There was a high prevalence of HIV among PWID, reaching 66% in 2006, decreasing to 48% in 2009 and 30% in 2016. This was a result of “combined prevention” programs including increased access to ART, methadone treatment, and harm reduction interventions (mainly information education communication, needle/syringe exchange

programs, and condoms), the estimated HIV incidence among PWID is now 0.8/100 person years.[8]

There is dearth of study on this subject of prevalence of psychiatric morbidities among opioid abusers & their severity in the states of North-Eastern India, particularly Tripura. Hence, the present study is a sincere effort in this direction.

MATERIALS AND METHODS:

The aim of the study was to compare anxiety and depression between intravenous and non-intravenous opioid abuser seeking treatment in a tertiary hospital in Tripura. The study sample consisted of a total of 140 number of study subjects who attended in psychiatric outpatient & indoor facilities of the department of Psychiatry, AGMC & GBP Hospital & the sample was taken by simple random sampling method. The duration of study was one and half years from January 2020 to June 2021. Sociodemographic information was gathered as per prepared standard questionnaire. Ethical approval & consent of the patients were obtained in the initial portion of the study. Informed written consent was obtained from the patients. The respondents were assured of confidentiality. The participants were clearly explained the purpose of the study and subjects were selected on voluntary basis.

Inclusion Criteria-

1. Opioid abusers attending outpatient Department (OPD) or admitted in inpatient department (IPD) of Department of Psychiatry of Agartala Government Medical College and GBP Hospital for its management.
2. Patients in the age group of 18-40 years
3. Patients consenting for the study.
4. Patients of all gender.

Exclusion Criteria-

1. Patients with age below 18 years or above 40 years.
2. Patients not consenting for the study.
3. Patients who have any systemic and chronic debilitating physical illness.

Tools Which Were Used In The Study Are:

- a) Informed consent form, b) proforma for socio demographic data c) ICD-10 Diagnosis Criteria d) Hamilton Anxiety Rating Scale (HAM-A) & e) Hamilton Depression Rating Scale (HAM-D)

Hamilton Anxiety Rating Scale (HAM-A): It is a psychological questionnaire used by clinicians to rate the severity of a patient's anxiety. The scale consists of 14 items designed to assess the severity of a patient's anxiety. Each of the 14 items contains a number of symptoms, and each group of symptoms is rated on a scale of zero to four, with four being the most severe. A rating of 1 indicates mild, 2 indicates moderate, 3 indicates severe and 4 indicates a very severe prevalence of the feeling in the patient. The compiled score ranges from 0 to 56. A score of 17 or less indicates mild, 18 to 24 indicates moderate and 25 to 30 indicates severe anxiety.

Hamilton Depression Rating Scale (HAM-D): is a multiple item questionnaire used to provide an indication of depression, and as a guide to evaluate recovery. The patient is rated by a clinician on 17 items. A score of 0-7 is considered to be normal while a score of 20 or higher is usually required for entry into a clinical trial.

RESULTS:

Table 1: Sociodemographic profile of the study population

Demographic details	No. of cases	Percentage
Age (in years)		
≤20	19	13.6
21-25	53	37.9
26-30	46	32.9
31-35	22	15.7
Total	140	100
Gender		
Male	133	95
Female	7	5
Marital status		
Married	38	27.10
Unmarried	102	72.90
Educational status		
Illiterate	04	2.9

Primary	10	7.1
Secondary	67	47.9
Higher Secondary	59	42.1
Religion		
Hindu	111	79.3
Christian	05	3.6
Muslim	24	17.1
Locality		
Rural	58	41.4
Urban	82	58.6
Occupation		
Self employed	34	24
Salaried	23	16
Farmer	16	11
Student	19	14
Unemployed	48	34
Mode of intake		
Intravenous	84	60
Non intravenous	56	40

Table 2: Distribution of anxiety of the study populations

Variable (HAM-A)	Frequency (n)	Percentage (%)
Mild	29	21
Moderate	15	11
Severe	96	69
Total	140	100

Table 3: Distribution of Depression of the study populations

Variable (HAM-D)	Frequency (n)	Percentage (%)
Mild	17	12
Moderate	29	21
Severe	13	09
None	81	58
Total	140	100

Table 4: Association between Age in Group & Mode of Intake

Mode of intake			
Age in Group	Intravenous	Non-Intravenous	TOTAL
≤20	15	4	19
Row %	78.9	21.1	100.0
Col %	17.9	7.1	13.6
21-25	36	17	53
Row %	67.9	32.1	100.0
Col %	42.9	30.4	37.9
26-30	24	22	46
Row %	52.2	47.8	100.0
Col %	28.6	39.3	32.9
>30	9	13	22
Row %	40.9	59.1	100.0
Col %	10.7	23.2	15.7
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous Intake group, 15 (17.9%) patients were ≤20 years old, 36 (42.9%) patients were 21-25 years old, 24 (28.6%) patients were 26-30 years old and 9 (10.7%) patients were 30 years old and above. In non-intravenous group, 4 (7.1%) patients were ≤20 years old, 17 (30.4%) patients were 21-25 years old, 22 (39.3%) patient were 26-30 years old and 13 (23.2%) patients were 30 years old and above.

Association of age in group with mode of intake was statistically significant ($p=0.0329$).

Table 5: Association between gender & Mode of Intake

Mode of intake			
Gender	Intravenous	Non-Intravenous	Total
Female	0	7	7
Row %	0.0	100.0	100.0
Col %	0.0	12.5	5.0
Male	84	49	133
Row %	63.2	36.8	100.0
Col %	100.0	87.5	95.0
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, all patients [84 (100.0%)] were male. In non-intravenous group, 7 (12.5%) patients were female and 49 (87.5%) patients were male. Association of sex with mode of intake was statistically significant ($p=0.0008$).

Table 6: Association between Religion & Mode of Intake

Mode of intake			
Religion	Intravenous	Non-Intravenous	TOTAL
Christian	0	5	5
Row %	0.0	100.0	100.0
Col %	0.0	8.9	3.6
Hindu	72	39	111
Row %	64.9	35.1	100.0
Col %	85.7	69.6	79.3
Muslim	12	12	24
Row %	50.0	50.0	100.0
Col %	14.3	21.4	17.1
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 72 (85.7%) patients were Hindu and 12 (14.3%) patients were Muslim. In non-intravenous group, 5 (8.9%) patients were Christian, 39 (69.6%) patients were Hindu and 12 (21.4%) patients were Muslim. Association of religion with mode of intake was statistically significant ($p=0.0083$).

Table 07: Association between Marital Status & Mode of Intake

Mode of intake			
Marital Status	Intravenous	Non-Intravenous	TOTAL
Married	12	26	38
Row %	31.6	68.4	100.0
Col %	14.3	46.4	27.1
Unmarried	72	30	102
Row %	70.6	29.4	100.0
Col %	85.7	53.6	72.9
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 12 (14.3%) patients were married and 72 (85.7%) patients were unmarried. In non-intravenous group, 26 (46.4%) patients were married and 30 (53.6%) patients were unmarried. Association of marital status with mode of intake was statistically significant ($p<0.0001$).

Table 08: Association between Locality & Mode of Intake

Mode of intake			
Locality	Intravenous	Non-Intravenous	TOTAL
Rural	40	18	58
Row %	69.0	31.0	100.0
Col %	47.6	32.1	41.4
Urban	44	38	82
Row %	53.7	46.3	100.0
Col %	52.4	67.9	58.6
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

Intravenous group, 40 (47.6%) patients were from rural area and 44 (52.4%) patients were from urban area. In non-intravenous group, 18 (32.1%) patients were from rural area and 38 (67.9%) patients were from urban area. Association of locality with mode of intake was not statistically significant ($p=0.0685$).

Table 09: Association between Family & Mode of Intake

MODE OF INTAKE			
Family	Intravenous	Non Intravenous	TOTAL
Joint	38	13	51
Row %	74.5	25.5	100.0
Col %	45.2	23.2	36.4
Nuclear	46	43	89
Row %	51.7	48.3	100.0
Col %	54.8	76.8	63.6
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 38 (45.2%) patients were from joint family and 46 (54.8%) patients were from nuclear family. In non-intravenous group, 13 (23.2%) patients were from joint family and 43 (76.8%) patients were from nuclear family. Association of family with mode of intake was statistically significant ($p=0.0079$).

Table 10: Association between Occupation & Mode of Intake

MODE OF INTAKE			
Occupation	Intravenous	Non Intravenous	TOTAL
Self Employed	33	1	34
Row %	97.1	2.9	100.0
Col %	39.3	1.8	24.3
Salaried	0	23	23
Row %	0.0	100.0	100.0
Col %	0.0	41.1	16.4
Farmer	10	6	16
Row %	62.5	37.5	100.0
Col %	11.9	10.7	11.4
Student	9	10	19
Row %	47.4	52.6	100.0
Col %	10.7	17.9	13.6
Unemployed	32	16	48
Row %	66.7	33.3	100.0
Col %	38.1	28.6	34.3
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 33 (39.3%) patients were self-employed, 10 (11.9%) patients were farmer, 9 (10.7%) patients were student and 32 (38.1%) patients were unemployed. In non-intravenous group, 1 (1.8%) patient was self-employed, 23 (41.1%) patients were salaried, 6 (10.7%) patients were farmer, 10 (17.9%) patients were student and 16 (28.6%) patients were unemployed. Association of occupation with mode of intake was statistically significant ($p<0.0001$).

Table 11: Association between Education & Mode of Intake

Mode of intake			
Education	Intravenous	Non Intravenous	TOTAL
Illiterate	4	0	4
Row %	100.0	0.0	100.0
Col %	4.8	0.0	2.9
Primary	10	0	10
Row %	100.0	0.0	100.0
Col %	11.9	0.0	7.1
Secondary	51	16	67
Row %	76.1	23.9	100.0
Col %	60.7	28.6	47.9
Higher Secondary	19	40	59
Row %	32.2	67.8	100.0
Col %	22.6	71.4	42.1
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In the intravenous intake group, 4 (4.8%) patients were illiterate, 10 (11.9%) patients had primary education, and 51 (60.7%) patients had studied up to secondary education and 19 (22.6%) patients had qualification of higher secondary and above. In non-intravenous group, 16 (28.6%) patients had secondary education, and 40 (71.4%) patients had qualification of higher secondary and above. Association of education with mode of intake was statistically significant ($p<0.0001$).

Table 24: Association between HAMA Score & Mode of Intake

Mode of intake			
HAMA Score	Intravenous	Non Intravenous	TOTAL
Mild	18	11	29
Row %	62.1	37.9	100.0
Col %	21.4	19.6	20.7
Moderate	8	7	15
Row %	53.3	46.7	100.0
Col %	9.5	12.5	10.7
None	58	38	96
Row %	60.4	39.6	100.0
Col %	69.0	67.9	68.6
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 18 (21.4%) patients had mild scores on HAM-A scale and 8 (9.5%) patients had moderate scores on HAM A scale. In non intravenous group, 11 (19.6%) patients had mild scores on HAMA scale and 7 (12.5%) patients had moderate scores on HAM A scale. Association of HAM A Score with mode of intake was not statistically significant ($p=0.8452$).

Table 25: Association between HAM D Score & Mode of Intake

MODE OF INTAKE			
HAM-D Score	Intravenous	Non Intravenous	TOTAL
Mild	17	0	17
Row %	100.0	0.0	100.0
Col %	20.2	0.0	12.1
Moderate	12	17	29
Row %	41.4	58.6	100.0
Col %	14.3	30.4	20.7
None	42	39	81
Row %	51.9	48.1	100.0
Col %	50.0	69.6	57.9
Severe	13	0	13
Row %	100.0	0.0	100.0
Col %	15.5	0.0	9.3
TOTAL	84	56	140
Row %	60.0	40.0	100.0
Col %	100.0	100.0	100.0

In intravenous group, 17 (20.2%) patients had mild scores on HAM D, 12 (14.3%) patients had moderate and 13 (15.5%) patients had severe HAM D scores. 42 (50%) patients did not have any depression as per the HAM D scale. In non intravenous group, 17 (30.4%) patients scored moderate depression on HAM D, and 39 (69.6%) did not have any depression. Association of HAM D score with mode of intake was statistically significant ($p<0.0001$).

DISCUSSION:

This cross-sectional comparative, descriptive study was conducted in the Department of Psychiatry, Agartala Government Medical College from January 2020 to June 2021. Patients included in the study were opioid abusers attending OPD or admitted to IPD for its management, within the age group of 18-40 years (both were inclusive) and consenting for the study. Total of 140 participants were included in the study.

In this study, 60% of the participants reported opioid intake by intravenous route while 40% reported non intravenous route of intake. According to this study, in intravenous mode of intake, 18 (21.4%) patients had mild anxiety and 8 (9.5%) patients had moderate anxiety. Whereas in the non intravenous mode of intake, 11 (19.6%) patients had mild anxiety and 7 (12.5%) patients had moderate anxiety. In this study none had severe anxiety. The findings were not statistically significant ($p=0.8452$). In the intravenous group, 17 (20.2%) patients had mild depressive symptoms, 12 (14.3%) patients had moderate and 13 (15.5%) patients had severe depressive symptoms. In non intravenous group, 17 (30.4%) patients had moderate depression. This was statistically significant ($p<0.0001$).

In this study 84 (60%) were intravenous opioid abusers and 56 (40%) were non intravenous opioid abusers. It was found that in intravenous mode of intake, 15 (17.9%) patients were ≤ 20 years old, 36 (42.9%) patients were 21-25 years old, 24 (28.6%) patient were 26-30 years old and 9 (10.7%) patients were >30 years old. In non intravenous mode of intake, 4 (7.1%) patients were ≤ 20 years old, 17 (30.4%) patients were 21-25 years old, 22 (39.3%) patients were 26-30 years old and 13 (23.2%) patients were >30 years old. This was statistically significant ($p=0.0329$).

CONCLUSION:-

The result showed strong correlation between depressive symptoms and opioid intake, which draws attention to the need of taking into consideration the comorbidity and its management. Clinicians should routinely assess for anxiety and depression in patients with opioid abuse disorders which tend to go undiagnosed and pose threat to one's livelihood and in turn increase substance taking behaviour. Early recognition and treatment of anxiety and depression associated with opioid abuse can lead to improved therapeutic outcome and may revert disastrous outcomes, including suicide. Prospective associations of depression with future drug use and impairment are not immediately evident, but could be examined in subsequent research. This study was

first of a kind in the state of Tripura, and I feel the need for more such studies with a view to detect psychiatric morbidities among drug abusers at the earliest, so that appropriate treatment can be initiated at the earliest and benefit to the patient can be maximized.

Limitations Of The Study:

The sample size was small. The study has been done in a single centre. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out. Ongoing COVID 19 pandemic and lockdown has further hampered the study.

REFERENCES:

- Ambekar A, Agrawal A, Rao R, Mishra AK, Khandelwal SK, Chadda RK on behalf of the group of investigators for the National Survey on Extent and Pattern of Substance Use in India (2019). Magnitude of Substance Use in India. New Delhi: Ministry of Social Justice and Empowerment, Government of India. 2019; 4:19-22.
- Witcher HU. Critical issues in the evaluation of comorbidity of psychiatric disorders. *Br J Psychiatry*. 1996; 30:9-16.
- S. Iskandar, R. Kamal, and C. A. De Jong, "Psychiatric comorbidity in injecting drug users in Asia and Africa," *Current Opinion in Psychiatry*, vol. 25, no. 3, pp. 213–218, 2012.
- F. L. Altice, A. Kamarulzaman, V. V. Soriano, M. Schechter, and G. H. Friedland, "Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs," *The Lancet*, vol. 376, no. 9738, pp. 367–387, 2010.
- R. Salo, K. Flower, A. Kielstein, M. H. Leamon, T. E. Nordahl, and G. P. Galloway, "Psychiatric comorbidity in methamphetamine dependence," *Psychiatry Research*, vol. 186, no. 2-3, pp. 356–361, 2011.
- J. A. Kelly, D. A. Murphy, G. R. Bahr et al., "Factors Associated With Severity of Depression and High-Risk Sexual Behavior Among Persons Diagnosed With Human Immunodeficiency Virus (HIV) Infection," *Health Psychology*, vol. 12, no. 3, pp. 215–219, 1993.
- D. Des Jarlais, P. M. Khue, J. Feelemyer et al., "Using dual capture/recapture studies to estimate the population size of persons who inject drugs (PWID) in the city of Haiphong, Vietnam," *Drug and Alcohol Dependence*, vol. 185, pp. 106–111, 2018.
- D. C. Des Jarlais, D. ThiHuong, K. ThiHaiOanh et al., "Prospects for ending the HIV epidemic among persons who inject drugs in Haiphong, Vietnam," *International Journal of Drug Policy*, vol. 32, pp. 50–56, 2016.
- Pradhan SN, Sharma SC, Shrestha MR, Shrestha S. A study of depression among patients of substance use disorder. *Journal of Kathmandu Medical College*. 2012;1(2):96-9.
- Mohanty R, Senjam G, Singh NH. Psychiatric comorbidities among opioid-dependent patients attending department of psychiatry, regional institute of medical sciences hospital, Manipur. *Indian Journal of Social Psychiatry*. 2018 Apr 1;34(2):132.
- Golden J, O'Dwyer AM, Conroy RM. Depression and anxiety in patients with hepatitis C: prevalence, detection rates and risk factors. *General hospital psychiatry*. 2005 Nov 1;27(6):431-8.
- Foley M, Schwab-Reese LM. Associations of state-level rates of depression and fatal opioid overdose in the United States, 2011–2015. *Social psychiatry and psychiatric epidemiology*. 2019 Jan;54(1):131-4.
- Yovtcheva SP, Rifai MA, Moles JK, Van Der Linden BJ. Psychiatric comorbidity among hepatitis C-positive patients. *Psychosomatics*. 2001 Sep 1;42(5):411-5.
- Mawiong AM, Senjam GS, Haobam M, Singh NH, Khongji P. A study of psychiatric comorbidities among treatment seeking opioid injectors attending tertiary care teaching hospital, Imphal for a period of 2 years. *Journal of Medical Society*. 2018 Sep 1;32(3):174.
- Fortier E, Alavi M, Bruneau J, Micallef M, Perram J, Sockalingam S, Dunlop AJ, Balcomb AC, Day CA, Treloar C, Bath N. Depression, anxiety, and stress among people with chronic hepatitis C virus infection and a history of injecting drug use in New South Wales, Australia. *Journal of addiction medicine*. 2017 Jan 1;11(1):10-8.
- Wang Z, Du J, Zhao M, Page K, Xiao Z, Mandel JS. Hepatitis C virus infection is independently associated with depression among methadone maintenance treatment heroin users in China. *Asia. Pacific Psychiatry*. 2013 Sep;5(3):191-6.
- Sullivan MD. Depression effects on long-term prescription opioid use, abuse, and addiction. *The Clinical journal of pain*. 2018 Sep 1;34(9):878-84.
- Scherer JF, Salas J, Copeland LA, Stock EM, Ahmedani BK, Sullivan MD, Burroughs T, Schneider FD, Bucholz KK, Lustman PJ. Prescription opioid duration, dose, and increased risk of depression in 3 large patient populations. *The Annals of Family Medicine*. 2016 Jan 1;14(1):54-62.
- Chalana H, Kundal T, Singh Malhari A. Depression as a Risk Factor for Relapse After Inpatient Opioid Detoxification: 1-Year Follow-Up Study. *International Journal of High Risk Behaviors and Addiction*. 2017 Sep 30;6(3).
- Mohamed II, Ahmad HE, Hassan SM. Assessment of anxiety and depression among substance use disorder patients: a case-control study. *Middle East Current Psychiatry*. 2020 Dec;27:1-8.
- Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Alcohol Research & Health*. 2006;29(2):107.
- Benningfield MM, Dietrich MS, Jones HE, Kaltenbach K, Heil SH, Stine SM, Coyle MG, Arria AM, O'Grady KE, Fischer G, Martin PR. Opioid dependence during pregnancy: relationships of anxiety and depression symptoms to treatment outcomes. *Addiction*. 2012 Nov;107:74-82.
- Brady KT, Haynes LF, Hartwell KJ, Killeen TK. Substance use disorders and anxiety: a treatment challenge for social workers. *Social work in public health*. 2013 May 1;28(3-4):407-23.
- Longo LP, Johnson B. Addiction: Part I. Benzodiazepines-side effects, abuse risk and alternatives. *American family physician*. 2000 Apr 1;61(7):2121.
- Buckingham E, Schrage E, Cournos F. Why the treatment of mental disorders is an important component of HIV prevention among people who inject drugs. *Advances in preventive medicine*. 2013 Jan 1;2013.
- Quinlan J, Cox F. Acute pain management in patients with drug dependence syndrome. *Pain reports*. 2017 Jul;2(4).
- Ghaddar A, Abbas Z, Haddad R. Opiate agonist treatment to improve health of individuals with opioid use disorder in Lebanon. *Harm reduction journal*. 2017 Dec;14(1):1-7.
- Mash DC, Duque L, Page B, Allen-Ferdinand K. Ibogaine detoxification transitions opioid and cocaine abusers between dependence and abstinence: clinical observations and treatment outcomes. *Frontiers in pharmacology*. 2018 Jun 5;9:529.
- Alves RL, Oliveira P, Lopes IM, Portugal CC, Alves CJ, Barbosa F, Summavielle T, Magalhães A. Early-life stress affects drug abuse susceptibility in adolescent rat model

- independently of depression vulnerability. *Scientific Reports*. 2020 Aug 7;10(1):1-1.
30. Conner KR, Pinquart M, Duberstein PR. Meta. analysis of depression and substance use and impairment among intravenous drug users (IDUs). *Addiction*. 2008 Apr;103(4):524-34.
 31. Nowotny KM, Perdue T, Cepeda A, Valdez A. Mental health of heroin users with differing injection drug use histories: A non-treatment sample of Mexican American young adult men. *Drug and alcohol dependence*. 2017 Dec 1;181:124-31.
 32. Pham Minh K, Vallo R, Duong Thi H, KhuatThiHai O, Jarlais DC, Peries M, Le SM, Rapoud D, Quillet C, NhamThi TT, Hoang Thi G. Psychiatric comorbidities among people who inject drugs in HaiPhong, Vietnam: the need for screening and innovative interventions. *BioMed research international*. 2018 Oct 4;2018.
 33. Adams M, Sionean C, Broz D, Lewis R, Wejnert C. Serious Mental Illness Among Young People Who Inject Drugs: An Assessment of Injection Risks and Healthcare Use. *The Journal of Infectious Diseases*. 2020 Oct 1;222(Supplement_5):S401-9.
 34. Væroy H. Depression, anxiety, and history of substance abuse among Norwegian inmates in preventive detention: reasons to worry?. *BMC psychiatry*. 2011 Dec;11(1):1-7.
 35. Markou A, Kosten TR, Koob GF. Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. *Neuropsychopharmacology*. 1998 Mar;18(3):135-74.
 36. Bojovic K, Simonovic J, Katanic N, Milosevic I, Pesic I, Delic D, Svrtlih N, Jevtovic DJ. The comparison of chronic hepatitis C treatment outcome between intravenous drug users and non-intravenous drug users. *Biomedicine & Pharmacotherapy*. 2013 Jul 1;67(6):517-20.
 37. James ME, Rubin CP, Willis SE. Drug abuse and psychiatric findings in HIVseropositive pregnant patients. *General hospital psychiatry*. 1991 Jan 1;13(1):4-8.
 38. Compton WM, Thomas YF, Stinson FS, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV drug abuse and dependence in the United States: results from the national epidemiologic survey on alcohol and related conditions. *Archives of general psychiatry*. 2007 May 1;64(5):566-76.
 39. Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results 83 from the National Epidemiologic Survey on Alcohol and Related Conditions. *Archives of general psychiatry*. 2007 Jul 1;64(7):830-42.
 40. Torres-Berrio A, Cuesta S, Lopez-Guzman S, Nava-Mesa MO. Interaction between stress and addiction: contributions from Latin-American neuroscience. *Frontiers in psychology*. 2018 Dec 21;9:2639.
 41. Vasylyev M, Davtyan H, Denisiuk O, Jayaraj J, Koval T, Piddubna A, Sluzhynska M, Sluzhynska O, Mulcahy F. Anxiety, depression, and quality of life among HIV positive injection drug users in Ukraine, 2017.
 42. Lemos VD, Antunes HK, Baptista MN, Tufik S, Mello MT, Formigoni ML. Low family support perception: a social marker of substance dependence. *Brazilian Journal of Psychiatry*. 2012 Mar;34(1):52-9.
 43. Arya A. Comparative study on depression & anxiety status of addict & Non addict in apex de-addiction & rehabilitation centre, Uttarakhand. *environment.*; 6: 7. 2018.
 44. Armstrong G, Nuken A, Samson L, Singh S, Jorm AF, Kermode M. Quality of life, depression, anxiety and suicidal ideation among men who inject drugs in Delhi, India. *BMC psychiatry*. 2013 Dec;13(1):1-1