RESEARCH

A study of predictors of retention to naltrexone maintenance therapy in patients with opioid use disorder: a prospective study

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Abstract

Objectives   Naltrexone prophylaxis is a well-established treatment for opioid use disorder. Our study aimed to track patients on naltrexone and investigate the factors predictive of retention.

Materials and methods   The study comprised 100 participants initiated on naltrexone, who underwent a 12-week follow-up. We analyzed a range of socio-demographic and clinical variables at 04 and 12 weeks to compare those who remained in treatment program with those who experienced relapse.

Results   The results revealed a predominantly young, unmarried, male, rural-dwelling sample with heroin as the primary opioid. Intravenous use was common (75%), with 57% of the participants exhibiting positive serology results for infections by hepatitis C (HCV), hepatitis B (HBV), and/or human immunodeficiency virus (HIV), and a significant proportion initiating opioids before the age of 20 (31%). The retention rates at 04 and 12 weeks were 83% and 64%, respectively. Several socio-clinical factors including age of initiation of use, rural residence, and comorbid psychiatric illness significantly influenced retention at 04 and 12 weeks.

Conclusion   The findings highlight the importance of tailored interventions that take into consideration the age, residence, socio-economic status, and psychiatric comorbidity to enhance retention rates. Identifying these factors can help improve the effectiveness of treatment programs and promote sustained recovery efforts.

Keywords   Naltrexone, Addiction, Heroin, Relapse

Introduction

Substance use is a behavior characterized by an individual experiencing a strong psychological and/or physiological desire to continue using a substance despite facing adversities, leading to prioritization of obtaining and using the substance over important aspects of life [1]. Substance use disorder (SUD) presents as a chronic illness marked by recurring patterns of recovery and relapse, frequent non-attendance at appointments, and untimely withdrawal from engagement, resulting in a progressive decline in the holistic health of both the patients and their familial support systems [2–4]. Opioid use disorder (OUD) is a significant public health issue, with fatal overdoses being a major concern. Other causes of mortality include suicide and blood-borne infections like hepatitis C (HCV), hepatitis B (HBV), and acquired immunodeficiency syndrome caused by HIV [5]. Recent studies estimate that globally, 40.5 million people are dependent on opioids, with approximately 109,500 deaths occuring due to opioid overdose, annually. [6, 7].

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Long-term management of OUD involves maintenance therapy, which utilizes medications like buprenorphine, methadone, or naltrexone (NTX) [8]. Research indicates that maintenance treatment offers advantages over alternative options such as detoxification, residential programs, behavioral therapies, or no long-term treatment [9, 10]. While buprenorphine and methadone have been the primary choices, there is a growing interest in examining the efficacy of alternative approaches such as NTX and slow-release oral morphine [11–14]. Naltrexone, an antagonist at mu-opioid receptors, was approved by the US FDA in 1984 for preventing relapse in OUD and can be administered orally or via intramuscular (IM) injection. It lacks reinforcing effects, making it suitable for individuals pursuing complete abstinence and an opioid-free lifestyle [15–17].

The concept of treatment retention serves a dual purpose, functioning both as a process and an outcome measure [18]. The assessment of treatment retention holds paramount importance across various domains: it facilitates the evaluation of treatment effectiveness, enables the optimization of interventions, assists in the efficient allocation of resources, enhances patient satisfaction and adherence, improves healthcare practices, and ensures the maintenance of ethical standards in healthcare delivery. Despite the huge burden of opioid dependence in India, there remains a significant gap in understanding the factors that influence individuals to stay engaged in treatment programs. Furthermore, no study has been conducted within our population; this study was initiated to address this gap.

Materials and methods

This study was a hospital-based study, conducted at the drug addiction center of a tertiary care hospital which has an in-patient facility for individuals with SUD. The study had a fair representation of the population from the entire region and was longitudinal and prospective in design, conducted over a period of 18 months. Consecutive recruitment of 100 participants diagnosed with OUD was done from the out-patient and in-patient departments of the center. The diagnosis of OUD was done using DSM-5 criteria, and the diagnosis was confirmed by the in-charge psychiatrist of the OPD/IPD. The participants were assessed at three times during the study: at the time of entry into the study (on the day of starting NTx), at 04 weeks, and 12 weeks afterward. Individuals were interviewed when they were stable, not in intoxication/withdrawal. Written informed consent was obtained in the local understandable language, and rigorous measures were taken to maintain confidentiality. Participants were briefed about the purpose of the interview, and incomplete interviews were not considered.

The inclusion criteria included (i) patients greater than 18 years of age, (ii) fulfilling the DSM-5 criteria for OUD, and those willing to participate in the study by providing written informed consent. The following participants were excluded: (i) those with acute intoxication, withdrawal, and/or delirium, (ii) those already on NTx; (iii) those having any contraindication to the use of NTx and those with a history of leprosy, tuberculosis, COPD, bronchial asthma, or severe liver disease.

Sample size

The sample size was determined using a formula with a 95% confidence interval, a 5% margin of error, and an anticipated prevalence of opioid use disorder based on previous studies, resulting in a calculated value of 80.

Study aims

  (i) To study the socio-demographic and clinical profile of patients initiated on oral Naltrexone.

 (ii) To determine the predictors of retention in patients on naltrexone at 04 and 12 weeks.

Operational definitions

a) Opioid use disorder: Opioid use disorder (OUD) is defined as a problematic pattern of opioid use leading to clinically significant impairment or distress. Diagnosis requires meeting at least two of eleven outlined criteria within 12 months, with severity categorized as mild (2–3 criteria), moderate (4–5 criteria), or severe (6 or more criteria) [19].

b) Relapse: relapse was defined as the recurrence of opioid use after a period of abstinence or control [20].

Measures

The following instruments were utilized in the study:

a) A semi-structured proforma was used to collect demographic data and clinical information on the age, residence, marital status, age of onset of use, duration of use, type of opioid, route of use, and serology status. At 04 and 12 weeks, the proforma also collected the side effect burden. This information was obtained through a semi-structured interview schedule.

b) Kuppuswamys Socio-demographic Scale: It is a measurement tool that calculates a composite score based on the education and occupation of the head of the family, and the monthly income of the household. The scale categorizes groups into five distinct social classes: Upper (I), Upper Middle (II), Lower Middle

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(III), Upper Lower (IV), and Lower (V) socio-economic status [21, 22].

c) The Mini-International Neuropsychiatric Interview is a structured diagnostic interview, with high reliability and validity, for DSM-5 and ICD-10 psychiatric disorders. It is designed to meet the need for a short and accurate structured psychiatric interview for multicenter clinical trials and epidemiological studies. This scale was used for the assessment of psychiatric comorbidities and all the diagnoses were confirmed by a consultant psychiatrist [23].

d) Clinical Opioid Withdrawal Score (COWS): It is a clinician-administered instrument that rates 11 common opiate withdrawal signs or symptoms. The summed score of these items can be used to assess a patient's level of opiate withdrawal. This tool can be used in both inpatient and outpatient settings [24].

e) Multidimensional Scale for Perceived Social Support (MDPSS): It is a 12-item questionnaire to identify an individual's perceived level of social support with family, friends, and significant others. It is a Likert type of scale and has demonstrated good reliability and validity across diverse populations [25].

f) Severity of Opioid Dependence Questionnaire (SODQ): It is a self-report assessment tool designed to measure the severity of opioid dependence in individuals, and comprises 14 items that assess various aspects of opioid dependence. It provides a quantitative measure of the severity. It has been widely used in both clinical and research settings and serves as a valuable tool [26].

Table 1 Socio-demographic characteristics of the sample

Variable	No. (%)
Age (in years)	
18–20	23 (23.0)
20–25	38 (38.0)
25–30	33 (33.0)
>30	06 (6.0)
Gender	
Male	99 (99.0)
Female	01 (1.0)
Educational **status**	
Primary	16 (16.0)
Higher secondary	42 (42.0)
Graduation	36 (36.0)
Post-graduation	06 (6.0)
Occupational status	
Employed	52 (52.0)
Unemployed	48 (48.0)
Socio-economic status	
Lower	41 (41.0)
Middle	11 (11.0)
High	48 (48.0)
Type of family	
Joint	36 (36.0)
Nuclear	64 (64.0)
Residence	
Rural	55 (55.0)
Urban	45 (45.0)
Marital status	
Married	21 (21.0)
Unmarried, single	79 (79.0)

Statistical analysis

Data was entered in Statistical Package for Social Sciences (SPSS) V27. Descriptive statistics was used for continuous variables and the chi-square and Fischer's exact test were applied for categorical variables. Group differences in scores were compared on the chi-square test and the Student's *t*-test. All *p*-values were two-sided, and *p*-value < 0.05 was considered statistically significant.

Results

Socio-demographic characteristics

The study sample consisted of 100 participants with a mean age of 23.45 ± 6.02 years. The majority of the participants were unmarried (79%), males (99%), from a rural background (55%), of middle socio-economic status (48%), employed (52%), and belonging to nuclear families (64%), as evident in Table 1.

Clinical characteristics

The primary opioid used by the participants was heroin, in 91 participants, accounting for 91% of the sample. Among all study participants, 09 individuals had a history of use of pharmaceutical opioids. Specifically, 03 patients exclusively used tramadol, 02 used tapentadol, and 04 used both tramadol and tapentadol. Seventy-five percent of the study population had intravenous as the major route of administration and 57% had positive serology tests for HCV, HBV, and/or HIV. Twenty-one percent of the sample had a history of comorbid medical illness, with hypertension (6%), diabetes (3%), and seizure disorder (3%) observed among participants, while 25% had a history of comorbid psychiatric illnesses with MDD, ADHD, and personality disorders being the commonest, seen in 11%, 4%, and 4% of the sample, respectively. As is evident from Table 2, 31% of the individuals had a history of early initiation of opioid use, before the age of 20 years. Seventy-nine percent of the sample had a

Table 2 Clinical characteristics

Variable	No. (%)
Type of opioid	
Heroin	91 (91.0)
Pharmaceutical opioid	09 (9.0)
• Tramadol	03 (3.0)
• Tapentadol	02 (2.0)
• Both	04 (4.0)
Route of use	
Non intravenous	25 (25.0)
Intravenous	75 (75.0)
Serology for HCV/HBV/HIV	
Positive	57 (57.0)
Negative	43 (43.0)
Family history of use of opioid	
Present	09 (9.0)
Absent	91 (91.0)
Comorbid medical illness	
Diabetes mellitus	03 (3.0)
Hypertension	06 (6.0)
Seizure disorder	03 (3.0)
Hypothyroidism	04 (4.0)
Multiple	05 (5.0)
Present	21 (21.0)
Absent	79 (79.0)
Comorbid psychiatric illness	
MDD	11 (11.0)
ADHD	04 (4.0)
BPAD	03 (3.0)
Personality disorders	04 (4.0)
Anxiety disorders	03 (3.0)
Present	25 (25.0)
Absent	75 (75.0)
Comorbid substance use	
Nicotine use	85 (85.0)
BZD use	23 (23.0)
Alcohol use	06 (6.0)
Multiple	17 (17.0)
Present	88 (88.0)
Absent	12 (12.0)
Duration of use (in years)	
< 1	19 (19.0)
1–5	50 (50.0)
> 5	31 (31.0)
Age of initiation of opioid use	
< 20 y	31 (31.0)
20 and above	69 (69.0)
Severity of dependence	
Mild	18 (18.0)
Moderate	26 (26.0)
Severe	56 (56.0)

Table 2 (continued)

Variable	No. (%)
COWS at the initiation of naltrexone	
Mild	21 (21.0)
Zero	79 (79.0)
Status at 1 month	
Retained	
Relapsed	
Status at 1 month	
Retained	83 (83.0)
Relapsed	17 (17.0)
Status at 3 months	
Retained	64 (64.0)
Relapsed	36 (36.0)

HCV hepatitis C, *HBV* hepatitis B, *HIV* human immunodeficiency virus, *MDD* major depressive disorder, *ADHD* attention deficit hyperactive disorder, *BPAD* bipolar affective disorder, *BZD* benzodiazepine, *COWS* Clinical Opioid Withdrawal Score

COWS score of 0 at the time of initiation of NTx. Severe dependence was seen in 56% of the study sample. Eighty-three percent of the participants were retained at 4 weeks and 64% at 12 weeks of oral naltrexone therapy.

Association of socio-clinical variables with retention at 4 weeks

Table 3 presents a comparison of socio-clinical variables between participants who were retained and those who experienced relapse at 4 weeks. The results indicate that socio-economic status ($x^2 = 11.09$, p-value < 0.01), residence ($x^2 = 3.213$, p-value = 0.07), and comorbid medical illness ($x^2 = 12.59$, p-value < 0.01) significantly influenced retention at 4 weeks. Additionally, participants who retained had a higher mean age ($T = 2.060$; CI = −5.58, −0.10; p-value = 0.04) and higher mean scores on MDPSS ($T = −5.420$; CI = −3.88, −1.80; p-value < 0.01) than patients who experienced relapse.

Association of socio-clinical variables with retention at 12 weeks

An early age of initiation of opioid use ($x^2 = 4.753$, p-value = 0.03), rural residence ($x^2 = 4.04$, p-value = 0.06), lower socio-economic status ($x^2 = 5.395$, p-value = 0.04), comorbid medical illness, ($x^2 = 10.85$, p-value < 0.01), comorbid psychiatric illness ($x^2 = 5.786$, p-value < 0.01), serology for HCV/HBV/HIV ($x^2 = 7.43$, p-value < 0.01), comorbid substance use ($x^2 = 2.952$, p-value = 0.08) significantly influenced retention on univariate analysis, as can be seen in Table 4. A higher mean age ($T = −1.62$; CI = −4.07, 0.24; p-value = 0.08), higher MDPSS score ($T = −8.208$; CI = −3.67, −2.24; p-value = 0.00), and a higher mean COWS score at baseline ($T = −2.192$;

Table 3 Association of socio-clinical variables with retention at 4 weeks

At 1 month	Retained (N = 83)	Relapsed (N = 17)	Chi-square/ T-value	Fischer's exact/ 95% CI	P-value
Age					
18–20	16 (19.3)	07 (41.2)			
20–25	32 (38.6)	06 (35.2)	4.767	0.260	0.19
25–30	29 (35.0)	04 (23.6)			
> 30	06 (7.2)	00 (0.0)			
Educational status					
Primary	13 (15.7)	03 (17.6)			
Higher secondary	32 (38.6)	10 (58.9)	3.34	0.378	0.50
Graduation	33 (39.7)	03 (17.6)			
Post-graduation	05 (6.0)	01 (5.9)			
Occupational status					
Employed	42 (50.6)	10 (58.9)	0.382	0.615	0.53
Unemployed	41 (49.4)	07 (41.1)			
Socio-economic status					
Lower	28 (33.8)	13 (76.5)			
Middle	44 (52.9)	04 (23.5)	11.09	0.005	**0.00**
High	11 (13.3)	00 (0.0)			
Type of family					
Extended	03 (3.7)	00 (0.0)			
Joint	29 (34.9)	04 (23.5)	1.668	0.662	0.43
Nuclear	51 (61.4)	13 (76.5)			
Residence					
Rural	49 (59.0)	06 (35.3)	3.213	0.107	**0.07**
Urban	34 (41.0)	11 (64.7)			
Marital status					
Married	20 (24.2)	02 (11.8)	1.250	0.514	0.26
Unmarried	63 (75.8)	15 (88.2)			
Type of opioid					
Heroin	75 (90.3)	16 (94.1)	0.243	1.000	0.62
Pharmaceutical	08 (9.7)	01 (5.9)			
Route of use					
Non intravenous	21 (25.3)	04 (23.5)	0.023	1.000	0.87
Intravenous	62 (74.7)	13 (76.5)			
Serology for HCV/HBV/HIV					
Negative	37 (44.6)	06 (35.3)	0.496	0.595	0.48
Positive	46 (55.4)	11 (64.7)			
Family history of opioid use					
Present	07 (8.4)	02 (11.8)	0.191	0.647	0.66
Absent	76 (91.6)	15 (88.2)			
Comorbid medical illness					
Present	12 (14.5)	09 (53.0)	12.59	0.001	**0.00**
Absent	71 (85.5)	08 (47.0)			
Comorbid psychiatric illness					
Present	21 (25.3)	04 (23.5)	0.023	1.00	0.87
Absent	62 (74.7)	13 (76.5)			
Comorbid substance use					
Present	74 (89.1)	14 (82.3)	0.618	0.423	0.43
Absent	09 (10.9)	03 (17.7)			

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Table 3 (continued)

At 1 month	Retained (*N* = 83)	Relapsed (*N* = 17)	Chi-square/ *T*-value	Fischer's exact/ 95% CI	*P*-value
Duration of use (in years)					
< 1	17 (20.4)	02 (11.8)	0.721	0.827	0.69
1–5	41 (49.4)	09 (53.0)			
> 5	25 (30.2)	06 (35.2)			
Age of initiation of use					
< 20 y	23 (27.7)	08 (47.0)	2.469	0.151	0.11
20 and above	60 (72.3)	09 (53.0)			
Severity of dependence					
Mild	13 (15.7)	05 (29.4)			
Moderate	20 (24.0)	06 (35.3)	3.730	0.130	0.15
Severe	50 (60.3)	06 (35.3)			
COWS score					
Mild	19 (22.9)	02 (11.8)	1.053	0.514	0.30
Nil	64 (77.1)	15 (88.2)			
Mean age	24.9 + 5.44	22.06 + 3.61	$T = -2.060$	−5.58, −0.10	**0.04**
Mean COWS score at baseline	21.7 ± 5.68	19.71 ± 3.54	$T = -1.388$	−4.84, 0.85	0.16
Mean SODQ scores at baseline	32.33 ± 7.85	33.29 ± 7.84	$T = (0.463)$	3.18, 5.11	0.64
Mean MDPSS score at baseline	10.9 ± 1.97	8.66 ± 1.91	$T = (-5.420)$	−3.88, −1.80	**0.00**

HCV hepatitis C, *HBV* hepatitis B, *HIV* human immunodeficiency virus, *COWS* Clinical Opioid Withdrawal Score, *SODQ* Severity of Opioid Dependence Questionnaire, *MDPSS* Multidimensional Scale for Perceived Social Support

CI = −4.62, −0.23; *p*-value = 0.03) favored retention at 12 weeks.

Discussion

Opioid dependence is a lifelong, chronic, relapsing, and remitting disorder. To keep these patients free from drugs, substantial therapeutic efforts are the need of the hour [27]. In general, treatment with methadone plays a critical role in the detoxification or maintenance of subjects with opioid dependence; however, methadone is not a perfect medicine, and some patients on methadone continue to abuse drugs and indulge in criminal activities [28]. Naltrexone is a long-acting opioid antagonist that is devoid of addiction and usually does not produce a sense of well-being. It is approved for use in the treatment of patients with opioid dependence [29]. Naltrexone is more suitable to prevent relapse in the category of patients in which poor compliance with treatment may have major consequences; these include health professionals, business executives, and individuals under legal supervision [30].

The present prospective study evaluated the retention rates and predictive factors (clinical and socio-demographic) for oral naltrexone in patients with opioid use disorder at a tertiary care teaching hospital in the northern part of the subcontinent. Studies have found variable results in medication compliance and retention rates with oral naltrexone [31].

Our study revealed several key findings: (a) predominant use of injection heroin, (b) high retention rates at 04 and 12 weeks with naltrexone, (c) an early age of initiation of opioid use, lower SES, comorbid psychiatric illness and high side effect rates affecting retention at 12 weeks, (d) no impact on retention at 4 and 12 weeks due to family type, residence, type of opioid, and severity of dependence or withdrawal.

The mean age of the participants was 23.45 years with a standard deviation of 6.02 years. The majority fell within the age range of 20 to 25 years, with only 6% being over 30 years old, consistent with findings from similar studies emphasizing the prevalence of substance use among early adults [32–39]. Almost all the participants were males, highlighting the challenges females face in treatment access due to lack of awareness and stigma. Studies have indicated that women face more difficulties in access to substance use treatment [33, 34]. The majority of participants were literate, unmarried, and living in nuclear families from rural areas, explained by the fact that Kashmir is predominantly rural and the sample primarily consisted of individuals in early adulthood, a demographic more likely to be educated. Additionally, living in nuclear families exposes individuals to increased life stresses without the support of extended family, potentially heightening vulnerability to substance use.

Early retention, at 04 weeks was seen in 83% of the patients with significant results in favor of various

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Table 4 Association of socio-clinical variables with retention at 12 weeks

At 3 months	Retained (*N*=64)	Relapsed (*N*=36)	Chi-square/*T*-value	Fischer's exact/95% CI	*P*-value
Age					
18–20	14 (21.8)	09 (25.0)			
20–25	25 (39.0)	13 (36.1)	4.116	0.250	0.24
25–30	19 (29.8)	14 (38.9)			
> 30	06 (9.4)	00 (0.0)			
Educational status					
Primary	10 (15.6)	06 (16.7)			
Higher secondary	23 (36.0)	19 (52.8)	3.577	0.441	0.46
Graduation	27 (42.2)	09 (25.0)			
Post-graduation	04 (6.2)	02 (5.5)			
Occupational status					
Employed	33 (51.6)	19 (52.8)	0.013	1.00	0.90
Unemployed	31 (48.4)	17 (47.2)			
Socio-economic status					
Lower	21 (32.8)	20 (55.6)	5.395	0.072	**0.06**
Middle	34 (53.1)	14 (38.9)			
High	09 (14.1)	02 (5.5)			
Type of family					
Extended	03 (4.7)	00 (0.0)			
Joint	21 (32.8)	12 (33.3)	1.751	0.670	0.41
Nuclear	40 (62.5)	24 (66.4)			
Residence					
Rural	40 (62.5)	15 (41.7)	4.04	0.060	**0.04**
Urban	24 (37.5)	21 (58.3)			
Marital status					
Married	16 (25.0)	05 (13.9)	1.815	0.218	0.17
Unmarried	48 (75.0)	31 (86.1)			
Type of opioid					
Heroin	57 (89.0)	34 (94.5)	0.81	0.482	0.36
Pharmaceutical	07 (11.0)	02 (5.5)			
Route of use					
Non intravenous	18 (28.1)	07 (19.4)	0.81	0.47	0.33
Intravenous	46 (71.9)	29 (80.6)			
Serology for HCV/HBV/HIV					
Negative	34 (53.1)	09 (25.0)	7.43	0.007	**0.006**
Positive	30 (46.9)	27 (75.0)			
Family history of opioid use					
Present	02 (3.1)	07 (19.4)	7.49	0.001	**0.006**
Absent	62 (96.9)	29 (80.6)			
Comorbid medical illness					
Present	07 (11.0)	14 (38.9)	10.85	0.001	**0.001**
Absent	57 (89.0)	22 (61.1)			
Comorbid psychiatric illness					
Present	11 (17.2)	14 (38.9)	5.786	0.028	**0.01**
Absent	53 (82.8)	22 (61.1)			
Comorbid substance use					
Present	59 (92.2)	29 (80.5)	2.952	0.118	**0.08**
Absent	05 (7.8)	07 (19.5)			

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Table 4 (continued)

At 3 months	Retained (*N*=64)	Relapsed (*N*=36)	Chi-square/*T*-value	Fischer's exact/95% CI	*P*-value
Duration of use (in years)					
<1	10 (15.6)	09 (25.0)			
1–5	32 (50.0)	18 (50.0)	1.719	0.419	0.42
>5	22 (34.4)	09 (25.0)			
Age of initiation of use					
<20 y	15 (30.6)	16 (44.4)	4.753	0.042	**0.03**
20 and above	49 (69.4)	20 (55.6)			
Severity of dependence					
Mild	10 (15.6)	08 (22.2)	1.542	0.511	0.46
Moderate	19 (29.7)	07 (19.5)			
Severe	35 (54.7)	21 (58.3)			
COWS score					
Mild	10 (15.6)	11 (30.5)	3.095	0.123	**0.07**
Nil	54 (84.4)	25 (69.5)			
Mean age	25.11 (5.98)	23.19 (3.42)	*T*=−1.762	−4.07, 0.24	**0.08**
Mean COWS score at baseline	22.23 (6.05)	19.81 (3.64)	*T*=−2.192	−4.62, −0.23	**0.03**
Mean SODQ scores at baseline	32.02 (8.31)	33.33 (6.89)	*T*=0.807	−1.92, 4.55	0.42
Mean MDPSS score at baseline	11.48 (1.54)	8.53 (2.02)	*T*=−8.208	−3.67, −2.24	**0.00**

HCV hepatitis C, *HBV* hepatitis B, *HIV* human immunodeficiency virus, *COWS* Clinical Opioid Withdrawal Score, *SODQ* Severity of Opioid Dependence Questionnaire, *MDPSS* Multidimensional Scale for Perceived Social Support

socio-demographic and clinical variables. Identification of these variables is important as this could help in the selection of suitable patients for long-term maintenance with naltrexone [40, 41]. Retention at 04 weeks was not significantly associated with occupation and marital status of the patient and serology status, comorbid psychiatric illness, type, and route of use of opioids, similar to results from other studies conducted [42–44]. However, rural residence, comorbid medical illness, and middle SES significantly impacted retention at 04 weeks. Participants with higher scores on the MDPSS scale also had a higher chance of retention.

There were many socio-clinical predictors significant on univariate analysis at 12 weeks, a later age of initiation, lower SES, and rural residence significantly predicted retention at 12 weeks. An early age of initiation of opioid use is associated with neurocognitive deficits including deficits in executive functions such as problem-solving, decision-making, and development of reward system and self-control, which could contribute to poorer retention [45]. It may be prudent to mention that such patients may benefit from more intensive treatment strategies, those aimed at assuring swift transition to and maintenance on naltrexone therapy [46].

Side effect score was predictive of retention at both 04 and 12 weeks, indicating that participants who develop side effects are more likely to relapse while on naltrexone. The most often reported adverse symptoms included

nausea, abdominal pain, trouble sleeping, headaches, low energy, depressed mood, and palpitations [47]. It may thus be considered that patients continue taking clonidine and other complementary medicines during the initial weeks of treatment [46]. Good social support also predicted retention at 04 and 12 weeks, similar to results from past studies [32, 47]. Generally, it is considered that participants who receive supervised medication have longer retention to treatment and supervision is an aid in treatment retention.

The severity of opioid dependence and severity of withdrawal symptoms did not significantly influence retention at 04 and 12 weeks in our study with similar results from many other studies highlighting that naltrexone could be a good treatment option in patients with severe dependence and dismissing the myth that patients retain in long-term treatment for prevention of withdrawals only [42].

The presence of a comorbid psychiatric illness predicted retention at 12 weeks with significantly lower retention in patients with comorbid psychiatric illness, which could be because patients with dual diagnosis have poor social support and a lack of insight into their drug-seeking behavior, leading to a poorer follow-up and thus retention. Patients with a comorbid psychiatric illness have worse substance use outcomes and poorer psychosocial functioning than those without, stressing the need for mental health assessment and treatment

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for psychiatric conditions in patients undergoing pharmacotherapy for opioid use disorders [43]. The common psychiatric illnesses found included mood disorders, personality disorders, and ADHD. Comorbid psychiatric illnesses also leads to some degree of socio-occupational dysfunction and loss of follow-up, translating into poorer retention. Patients with comorbid substance use also had poorer retention to therapy; this is a well-known fact that people with dependence on multiple substances have poorer outcomes than the ones with single substance use.

Employment, marital status, and type of family were not found to be predictors of retention at 04 and 12 weeks. Studies have found that the retention rates were better among those who were employed, married, and living in a joint family type highlighting the possible role of family and spouse support in ensuring treatment adherence [48, 49]. However, our study failed to demonstrate such association.

Residence was also not found to be a predictor of retention at 12 weeks, a longer distance to the treatment center implies a longer time needed to commute to get prescription medicine which might act as a deterrent against follow-up. This scenario is true for rural settings in the subcontinent [50–52]. However, in the present study, distance of residence from the treatment center was not found to be predictive of retention at 12 weeks which could be because NTX is available at the treatment center and is provided for longer durations of time when required. Lower socio-economic status was found to be predictive of retention at 12 weeks but not 04 weeks.

The route of use and type of opioid used also did not impact retention significantly; however, positive serology status was found to be a positive predictor of retention at 12 weeks. Positive serology for HCV/HBV/HIV in opioid use has been strongly associated with impulsivity and the presence of high-risk behaviors like sharing of paraphernalia and unprotected sexual intercourse. Patients with impulsivity have higher chances of becoming non-compliant with therapy and relapse [17].

There is a need for a long-term follow-up study to assess sustained effectiveness in comparison with other treatments, and explore factors influencing retention. Studies should also focus on elucidation of underlying mechanisms of action and implementation to optimize real-world utilization, all aimed at enhancing treatment outcomes for OUD.

Strengths
The strengths of the current study lie in its high baseline completion rate, extensive assessment of heroin users, and comprehensive analysis of multiple and varied clinical and psychosocial predictors, offering valuable insights into retention on naltrexone treatment in this population.

Limitations
The assessment was conducted at a single center so the findings cannot be generalized to the community. The sample size was relatively small and cannot be considered representative of the entire North Indian population. Small sample sizes may also lead to type II errors and cause overestimation. The study design, although prospective, was a non-randomized one with the absence of a control arm; this could potentially lead to selection bias.

Conclusion
In conclusion, lower age of initiation (odds ratio = 4.3), lower socio-economic status (OR = 1.6), comorbid psychiatric illness (OR = 3.1), and additional substance use (OR = 5.2) were predictors for poor retention to naltrexone maintenance therapy in subjects with opioid use at 12 weeks of oral naltrexone therapy.

Declarations

Ethics approval and consent to participate
The research work was initiated only after approval by the Institutional Ethical Committee, GMC Srinagar. Only those were taken for the study who gave the informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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