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Original Article

Prevalence & predictors of sexual functioning & sex hormone profiles among men with opioid dependence: A community-based, cross-sectional study

Vinit Patel[1,3], Ravindra Rao[1], Roshan Bhad[1], Ashwani Kumar Mishra[1], Rizwana Quraishi[1] & Yashdeep Gupta[2]

[1]National Drug Dependence Treatment Centre, & [2]Department of Endocrinology, All India Institute of Medical Sciences, New Delhi & [3]Department of Psychiatry, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

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***Background & objectives*: Though sexual dysfunction are common in individuals with opioid dependence, the relative contribution of hormonal and psychological determinants remains unclear. Studies assessing sexual functioning and sex hormone levels together in this population remain limited. This study aimed to evaluate self-reported sexual dysfunction and sex hormone alterations, and their association with demographic, psychosocial, and hormonal factors in men with opioid dependence, primarily using heroin.**

***Methods*: In this cross-sectional study, 143 sexually active males (aged 18-50 yr) with opioid dependence were recruited. Sexual functioning was assessed using the international index of erectile function (IIEF-15). Hormonal assays included total testosterone, prolactin (PRL), luteinising hormone (LH), follicle-stimulating hormone (FSH), gonadotropin-releasing hormone (GnRH), sex hormone-binding globulin (SHBG), and dehydroepiandrosterone sulphate (DHEA-S). Descriptive statistics, Spearman's rank correlation with FDR (false discovery rate) correction, and hierarchical multiple regression with bootstrapped confidence intervals (1000 samples) were conducted. A sensitivity analysis restricted to married participants (n=78) allowed inclusion of intimate partner violence as predictor.**

***Results*: The median age of participants (n=143) was 26 yr [Interquartile range (IQR):24-30], with 93 per cent identifying as heterosexual. Erectile dysfunction (93.7%, n=134), orgasmic dysfunction (95.1%, n=136), low sexual desire (94.4%, n=135), dissatisfaction with sexual intercourse (99.3%, n=142), and premature ejaculation (72%, n=103) were highly prevalent. Hormonal analysis showed low testosterone in 7.7 per cent (n=11), high PRL in 8.4 per cent (n=12), and elevated GnRH in 57.3 per cent (n=82) of participants. Median hormone levels were: Testosterone 20.5 (15.0-27.3) nmol/L, PRL 5.8 (3.5-11.2) ng/mL, and GnRH 160.3 (132.2-178.1) pg/mL. No significant correlations were observed between hormone levels and sexual function. In regression analysis, demographic and psychosocial variables predicted**

Opioid dependence is a major global health challenge, accounting for most drug-related deaths and disability[1]. In India, around two per cent of the population reported past-year opioid use, with heroin being the most commonly used opioid (1.14%), followed by pharmaceutical opioids (0.96%), and

sexual functioning, while hormonal measures did not contribute independently. The final model explained 17 per cent of variance (adjusted R^2 = 0.17).

***Interpretation & conclusion*: Sexual dysfunction in men with opioid dependence primarily using heroin was driven more by psychosocial and demographic determinants than by hormonal changes. Endocrine alterations were not sufficient to explain the high burden of dysfunction. Addressing sexual health in opioid dependence requires a multifactorial approach, with attention to social and psychological contributors alongside biological assessment.**

Key words Erectile dysfunction - gonadotropin releasing hormone - heroin dependence - sex hormones - sexual dysfunction, physiological - testosterone

opium (0.52%)[2,3]. Opioid dependence has significant adverse effects on physical health of the user, including high risk of HIV and infective hepatitis.

Opioid dependence is also associated with adverse sexual health, affecting both sexual functioning and sex hormone levels[4]. Sexual functioning problems include erection difficulties, decreased libido, premature ejaculation, orgasmic difficulties, and dissatisfaction with sexual activity[5,6]. Their prevalence varies widely (14%-92%), depending on study methods and population characteristics[5,7,8]. Most research has examined individuals who are on opioid agonist treatment, particularly methadone or buprenorphine[9-13]. Fewer studies have assessed sexual functioning among individuals currently using illicit opioids[7,14]. While individuals on opioid agonist treatment have constant levels of opioids in their blood, those using illicit opioids would go through cycles of intoxication and withdrawals. This may impact sexual functioning differently[15].

Opioids disrupt the hypothalamic-pituitary-gonadal (HPG) axis, suppressing gonadotropin-releasing hormone (GnRH) secretion. This, in turn, lowers gonadotropin and testosterone levels, while elevating prolactin level, both of which contribute to erectile dysfunction, reduced libido, and orgasmic difficulties[4,16-18]. While testosterone suppression and hyperprolactinemia are well established, research on luteinising hormone (LH) and follicle-stimulating hormone (FSH) remains limited. Studies in individuals on opioid agonist treatment have reported gonadotropins within normal range[19,20]. No previous study has systematically reported GnRH levels in opioid users.

Studies in India have primarily focused on sexual functioning problems, using convenient and small samples. These studies report prevalence of erectile dysfunction ranging from 53 per cent to 92 per cent[21-24]. We could not find any study from India that has assessed sex hormone levels among individuals with opioid dependence. We aimed to assess sexual functioning and sex hormone levels in untreated men with opioid dependence, actively using heroin. We also explored potential correlations between hormonal measures and domains of sexual functioning.

Materials & Methods

The study was carried out in a community drug treatment clinic, All India Institute of Medical Sciences (AIIMS), a tertiary care hospital at New Delhi, India. Data for the present paper were collected from January 1, 2023 to October 31, 2023. The study was approved by the Institutional Ethics Committee (IEC) for postgraduate research. All participants provided written informed consent after being explained study's objectives, and procedures. Confidentiality was ensured by de-identifying participants' data and storing it in a password-protected database. Participants who screened positive for comorbid psychiatric or medical disorders received psychoeducation and were referred for appropriate clinical care. The study adhered to the Declaration of Helsinki.

Study design: This study is part of a larger longitudinal cohort study with a three-month follow up assessment; however, the present paper focuses only on the baseline findings from the original study. This community clinic at NDDTC, AIIMS specialises in treatment of opioid dependence, offering methadone and buprenorphine-based opioid agonist treatment (OAT). It serves a catchment area of 5-7 km radius, catering to ~1,000 patients per month. New patients are registered twice a week, while follow up visits are available on six working days.

Study population and sampling: The study population included patients diagnosed with opioid dependence (ICD-11: 6C43.2, WHO 2022) and seeking treatment at the community drug treatment clinic. All newly registered patients meeting the selection criteria were invited to participate in the study; those providing written informed consent were enrolled in the study. The original sample size was calculated for the longitudinal cohort design, which required 72 participants completing follow-up for adequate paired analysis. Anticipating 50 per cent dropout rate, we set a baseline recruitment target of 144 participants, and 143 were ultimately enrolled. As the present analysis reports only baseline cross-sectional data, we additionally conducted a post-hoc power and precision check using *G**Power (Exact test family, correlation: bivariate normal model, two-tailed). Given the clinic's fixed registration days and structured intake process, every eligible patient was approached consecutively, ensuring strict consecutive sampling.

Selection criteria: Eligible participants were men, within the age group of 18-50 yr, sexually active in the past three months (defined as at least one sexual intercourse with a partner), using heroin as their primary opioid for at least 25 days in the past month, newly registered at the clinic for receiving OAT, not on treatment for opioid dependence in the past month, and willing to provide blood and urine samples at baseline and follow-up. Exclusion criteria included severe mental illness affecting their ability to participate, harmful use or dependence on other psychoactive substances (except nicotine) in the past three months, presence of chronic medical or endocrinological conditions, and use of any medications affecting sexual functioning or sex hormone levels in the past three months (such as antidepressants, antipsychotics, hormonal replacements, and anabolic steroids).

Data collection: All participants were interviewed in a private setting by the first author, in a single session. Data were collected using a semi-structured proforma covering socio-demographic, substance use, clinical, and sexual history (sexual orientation, age at first intercourse, partners' gender/type, number of partners, sexual practices, sexually transmitted infections, intercourse under intoxication, substances used to enhance performance, premature ejaculation history, privacy, and partner's substance use). The standardised instruments included:

- *Alcohol, smoking, and substance involvement screening test (ASSIST 3.0)*: It was used for assessing substances use other than opioids[25]. Those with scores of ≥11 for alcohol and ≥4 for other psychoactive substances (denoting harmful or dependent use) were excluded from the study.
- *Leeds dependence questionnaire (LDQ)*: It was used to measure opioid dependence severity over the last week. A score >20 indicates severe dependence[26].
- *The International index of erectile function (IIEF-15)*: It was used to assess sexual functioning, covering five domains (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). Each item is scored on a Likert scale, with higher scores indicating better sexual function. The IIEF-15 had acceptable internal consistency ($\alpha > 0.70$) and test-retest reliability ($r > 0.70$), except for the orgasmic function scale[27].
- *Fagerström test for nicotine dependence (FTND/ FTND-ST)*: These were used to assess nicotine dependence severity for smoking and smokeless tobacco respectively[28,29].
- *Clinical opiate withdrawal scale (COWS)*: It was used for opioid withdrawal severity[30].
- *Depression, anxiety, and stress scale (DASS-SF)*: It was used to evaluate depression, anxiety, and stress symptoms. It gives a total raw score, along with three subdomain raw scores for depression, anxiety, and stress[31].
- *HIV risk taking behaviour scale (HRBS)*: It is an 11-item, clinician-rated tool measuring risky behaviours among injection drug users (IDU) related to HIV transmission[32].

Sample collection: Blood and urine samples were collected from each participant at both time points using aseptic precautions. The samples were transported, processed, analysed, and stored at -80°C for further testing. Blood samples (10 mL) were drawn, prior to initiation of opioid agonist therapy, between 8:00 - 11:00 AM for haematological, biochemical, and hormonal assays. Most had last used heroin in the early morning prior to attending the clinic and were either intoxicated or about to enter early withdrawal at the time of sampling. Hormonal assays were conducted using electrochemiluminescence immunoassay (ECLIA) for serum-based hormones. GnRH was analysed separately using enzyme-linked immunosorbent assay (ELISA) in plasma.

Data management and statistical analysis: Data were managed using REDCap (research electronic data

capture)[33,34], and statistical analysis was performed using licensed IBM-SPSS statistics for Windows, Version 29.0.2.0 (IBM Corp, Armonk, NY). Continuous data were summarised using mean (standard deviation) or median (interquartile range) based on the data distribution, while frequencies (percentages) were used for categorical variables. The normality of continuous data was assessed using Shapiro-Wilk test. Given that most continuous variables were not normally distributed, non-parametric tests were used for analysis. Spearman's rank correlation was used to assess the relationship between the sexual functioning scores and sex hormone levels. A two-sided *P* value of <0.05 was considered statistically significant for all analyses.

The false discovery rate (FDR) correction using the Benjamini-Hochberg method was applied to adjust for multiple comparisons, ensuring control over Type I errors (adjusted $P<0.00125$).To examine whether hormonal variables independently predicted sexual functioning after accounting for other covariates, hierarchical multiple linear regression was conducted with IIEF total score as the dependent variable. Predictors were entered in four blocks: (*i*) demographics (age, education, occupation, marital status), (*ii*) opioid use variables (duration of use, daily expenditure, LDQ score), (*iii*) psychosocial/confounder variables (DASS total, HIV risk-taking, FTND), and (*iv*) hormones (total testosterone, prolactin, GnRH, DHEAS). In addition to the full-sample model, a sensitivity analysis restricted to married participants was conducted to include intimate partner violence (IPV) as an additional psychosocial predictor. Regression assumptions (linearity, homoscedasticity, collinearity) were checked and adequately met. Because residual normality was not satisfied, robust confidence intervals were estimated using bias-corrected accelerated (BCa) bootstrapping with 1000 samples.

Results

A total of 143 participants were enrolled. With n=143, the study had ~82 per cent power to detect correlations of $r \geq 0.23$ at $\alpha=0.05$. For prevalence estimation, the 95 per cent confidence interval for erectile dysfunction (93.7%) was 88.5-96.7 per cent, indicating good precision. These findings confirm that the achieved baseline sample size was adequate for the cross-sectional objectives of prevalence estimation and correlation analysis.

Table I. Socio-demographic details of participants with opioid dependence (n=143)

Demographic characteristics	n (%)
Education status	
Not formally educated	15 (10.5)
Primary	23 (16.1)
Middle, high, intermediate	90 (63.0)
Graduate and above	15 (10.5)
Marital status	
Unmarried	64 (44.8)
Married, Living together	77 (53.8)
Married, separated/ divorced	2 (1.4)
Employment status	
Never employed	3 (2.1)
Unemployed	32 (22.4)
Part time	30 (21.0)
Full time	78 (54.5)
Current occupation	
Unskilled	44 (40.7)
Skilled	62 (57.4)
Professional	2 (1.9)
Joint family	72 (50.3)
Others	71 (49.7)

Socio-demographic characteristics: The median (IQR) age of the study participants was 26 (24-30) years. The socio-demographic of the participants details are provided in table I.

Opioid and other substance use history: The median age of onset for heroin use was 19 years (IQR 17-24). All the participants reported using heroin by inhalational route (smoking or chasing) in their lifetime. About 19.6 per cent (n=28) reported injecting heroin at some point in life, and 7 per cent (n=10) had injected heroin in the past month. Participants reported near-daily heroin use, with an average of 29.5 days (SD = 1.2) of use in the past month. The median LDQ score was 27 (IQR 26-28), indicating severe OD.

About 7.7 per cent (n=11) reported lifetime dependence on alcohol, 1.4 per cent (n=2) on cannabis, and 88.8 per cent (n=127) on tobacco. About 93 per cent (n=133) participants were classified as moderate-risk and 6.3 per cent (=9) as high-risk for tobacco use according to ASSIST scores. According to ASSIST scores, all participants (100%, n=143) were classified as high-risk for opioid use.

All, except one, 142 participants reported current tobacco smoking. Based on the Fagerström test for nicotine dependence (FTND), 31 (21.8%) had low dependence, 24 (16.9%) had low-to-moderate dependence, 65 (45.8%) had moderate dependence, and 22 (15.5%) had high dependence. Among the 97 participants who reported smokeless tobacco use, 18 (18.6%) had low dependence, 25 (25.8%) had low-to-moderate dependence, 20 (20.6%) had moderate dependence, and 34 (35.1%) had high dependence. DASS-21 scores indicated that none of the participants had depression, anxiety, or stress. No participant was receiving psychotropics or hormonal agents at baseline, consistent with the exclusion criteria.

Marital history: About 55.2 per cent (n=79) were married [average frequency of marriage once (IQR 1-1)] and had one child (IQR 0-2). Among married participants, 87.3 per cent (n=69) reported being 'very happy' in their marriage, 3.8 per cent (n=3) as 'happy,' and 8.9 per cent (n=7) as 'very unhappy.' Among married participants, 81 per cent (n=64) reported perpetrating intimate partner violence (IPV), with verbal abuse being most common (79.7%, n=63), followed by physical abuse (50.6%, n=40), and sexual abuse (19.0%, n=15). Conversely, 39.2 per cent (n=31) of participants reported experiencing IPV from their partners, with verbal abuse being the most common, reported by all (39.2%, n=31), followed by physical abuse (6.3%, n=5). None reported experiencing sexual abuse from their partners.

Sexual history: Majority of the participants (93%, n=133) identified themselves as heterosexual in orientation and 7 per cent (n=10) as bisexual. The median age at first sexual intercourse was 17 yr (IQR 14-18), and the median time since last sexual intercourse was 7 days (IQR 3-30). All participants reported having female sex partners over their lifetime; 6.3 per cent (n=9) reported having male partners and 7.7 per cent (n=11) having transgender partners. In the last three months, all the participants had female sex partners, and 1.4 per cent (n = 2) had transgenders as sex partners.

About 55.2 per cent (n=79) engaged in sexual activity with their wives, 50.3 per cent (n=72) with girlfriend, 46.2 per cent (n=66) with FSWs, and 11.2 per cent (n=16) with men in their lifetime. In the past three months, 53.8 per cent (n=77) engaged in sexual activity with their wives, 28 per cent (n=40) with girlfriend, 18.9 per cent (n=27) with casual partners (females other than wife and girlfriend), and 17.5 per cent (n=25) with FSWs. Only 1.4 per cent (n=2) reported having sex with males in the past three months. Among the 66 participants who reported lifetime sexual intercourse with FSWs, 9.1 per cent (n=6) had unprotected intercourse. The majority of participants (93%, n=133) reported having had sexual intercourse under the influence of drugs at some point. Opioids were the most commonly involved substance during these encounters (97%, n=129), followed by alcohol (2.3%, n=3) and cannabis (0.8%, n=1). One-fourth of the participants (25.2%, n=36) reported using any over-the-counter medications, while more than half (55.9%, n=80) specifically used heroin for enhancing their sexual performance. Additionally, 6.3 per cent (n=9) of participants reported that their sexual partners use any psychoactive substances, with opioids (4.2%, n=6) and alcohol (2.1%, n=3) being the most common. Notably, all participants in this group (6.3%, n=9) had engaged in sexual intercourse while their partner was under the influence of drugs.

Sexual functioning and sex hormones: Erectile dysfunction (ED) was reported by 93.7 per cent (n=134) participants, while 95.1 per cent (n=136) had difficulty in achieving orgasm. About 94.4 per cent (n=135) reported decreased libido, while 99.3 per cent (n=142) expressed dissatisfaction in sexual intercourse. About 88.8 per cent (n=127) reported overall dissatisfaction with their sexual experiences. Premature ejaculation (defined as intravaginal ejaculatory latency time (IELT) of less than 2 min) was reported by 72 per cent (n=103) participants. Severity stratification of various domain of sexual dysfunction is shown in figure. Levels of sex hormones are shown in table II.

Correlations between sexual functioning and hormonal levels: Spearman's rank correlation analysis revealed no significant relationship between most sexual functioning domains and sex hormone levels. However, LH showed a weak negative correlation with erectile function (ρ_s=-0.237, P=0.034), but this association did not remain statistically significant after FDR correction for multiple comparisons (adjusted P value <0.00125). No other sexual functioning domains showed significant correlations with hormone levels. (Supplementary Table I).

Hierarchical regression analyses: Hierarchical regression results are shown in supplementary tables II-V. In the full-sample model (N=143), demographic

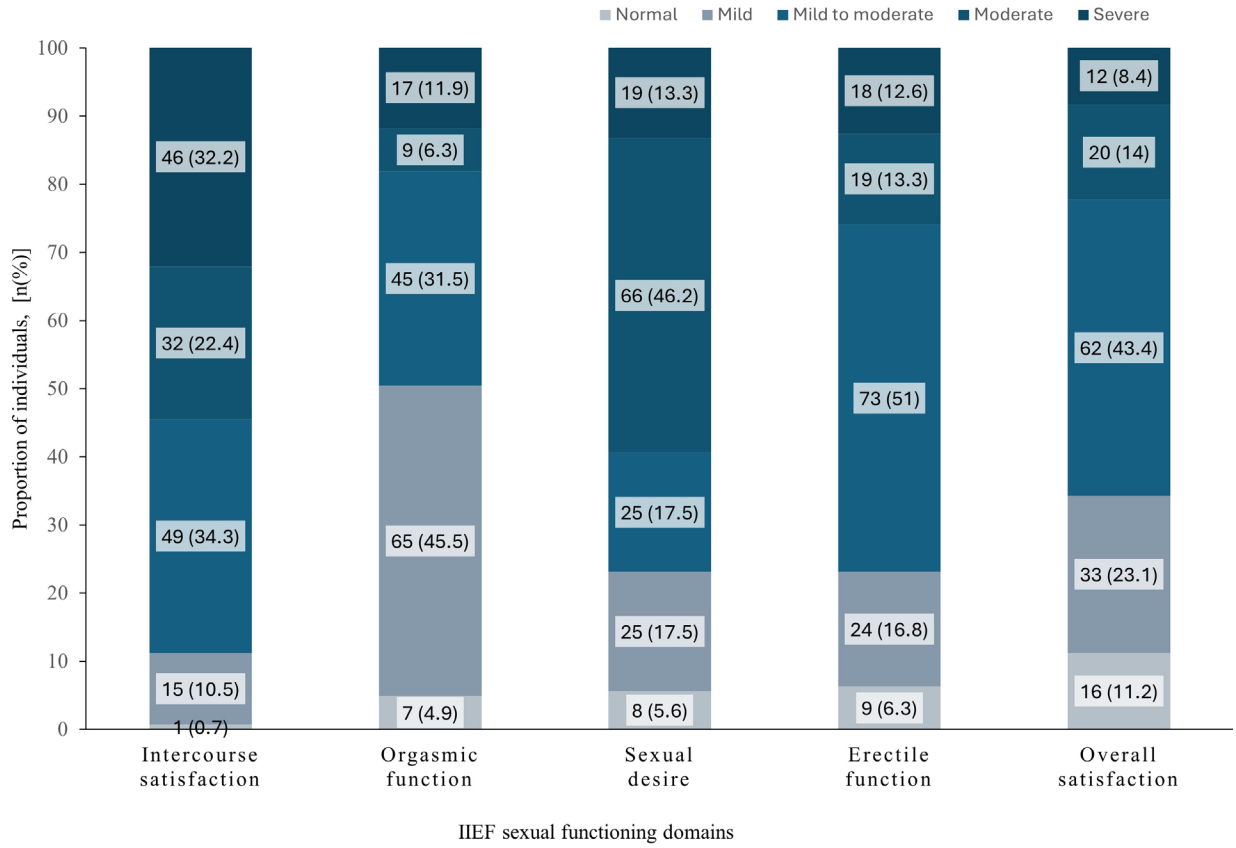

Figure. Severity of sexual dysfunction as per IIEF-15. The image presents the classification of male sexual dysfunction across five domains using validated scoring criteria. Erectile dysfunction (total score 1-30) is categorised into normal (25-30), mild (19-24), mild to moderate (13-18), moderate (7-12), and severe (1-6). Orgasmic dysfunction (total score 1-10) is classified as normal (9-10), mild (7-8), mild to moderate (5-6), moderate (3-4), and severe (1-2). Reduced sexual desire (total score 2-10) follows a similar classification with normal (9-10), mild (7-8), mild to moderate (5-6), moderate (3-4), and severe (2). Intercourse dissatisfaction (total score 0-15) is categorised as normal (13-15), mild (10-12), mild to moderate (7-9), moderate (4-6), and severe (0-3). Lastly, overall dissatisfaction (total score 2-10) is classified into normal (9-10), mild (7-8), mild to moderate (5-6), moderate (3-4), and severe (2).

factors explained 13 per cent variance in IIEF scores (R^2=0.133), with marital status (β=0.31, *P*=0.002) and occupational status (β=0.18, *P*=0.031) as significant predictors. Adding opioid variables modestly improved the model (ΔR^2=0.045, *P*=0.07), with education emerging as significant (β=0.16, *P*=0.048) and LDQ showing a borderline negative association. Inclusion of psychosocial variables further improved fit (ΔR^2=0.057, *P*=0.024), with HIV risk-taking emerging as a consistent positive predictor (β=0.25, *P*=0.003). In the final block, hormones (total testosterone, prolactin, GnRH, DHEAS) did not improve the model (ΔR^2=0.015, *P*=0.63) and none were significant predictors. The final model explained 17 per cent of variance (Adj R^2=0.17). Bootstrapped CIs confirmed these findings, with no change in significance patterns (Supplementary Table IV).

A sensitivity analysis restricted to married participants (N=78) allowed inclusion of IPV. In this model, IPV emerged as a significant negative predictor of IIEF scores (β=-0.29, *P*=0.016), while other psychosocial and hormonal variables were not significant. Bootstrapped regression confirmed this association (*P*=0.019; Supplementary Table V). Thus, across both models, demographic and psychosocial factors (marital status, occupation, HIV risk-taking, IPV) were more strongly associated with sexual functioning than hormonal measures.

Discussion

This study examined sexual functioning and sex hormone profiles among treatment-naïve males with opioid dependence in a community treatment setting in India. We found a high prevalence of sexual dysfunction across all domains (erectile, orgasmic, desire, and satisfaction). Hormonal disruptions such as elevated GnRH, low prolactin, and low DHEAS was also seen, while testosterone was normal in most

Table II. Sex hormones levels among the participants (N=143)

Hormone (normal range)	Median (IQR)			
		Less than normal, n (%)	Normal, n (%)	More than normal, n (%)
Total testosterone (TT) (8.33 to 30.19 nmol/L)	20.5 (15.0-27.3)	11 (7.7)	109 (76.2)	22 (15.4)
Free testosterone index (FTI)[#] (24.5 to 113.3%)	57.5 (43.2-78.9)	8 (5.6)	115 (80.4)	19 (13.3)
Sex hormone binding globulin (SHBG) (16.2 to 68.5 nmol/L)	34.2 (24.1-47.6)	17 (11.9)	120 (83.9)	5 (3.5)
Luteinising hormone (LH) (0.57 to 12.07 mIU/mL)	2.6 (1.8-4.2)	2 (1.4)	138 (96.5)	2 (1.4)
Follicle stimulating hormone (FSH) (0.95 to 11.95 mIU/mL)	2.9 (2.1-4.4)	6 (4.2)	134 (93.7)	2 (1.4)
Gonadotropin releasing hormone (GnRH)* (19 to 154 pg/mL)	160.3 (132.2-178.1)	0	61 (42.7)	82 (57.3)
Prolactin (PRL) (3.46 to 19.4 ng/mL)	5.8 (3.5-11.2)	35 (24.5)	95 (66.4)	12 (8.4)
Dehydroepiandrosteronesulfate (DHEAS)[+](45.1 to 447.6 µg/dL)	183.2 (118.1-274.1)	66 (46.2)	75 (52.4)	1 (0.7)

*-measure in plasma sample, + age specific normal range, normal range shown for the age group of our sample, [#]-FTI = (TT/SHBG)*100

participants. No significant correlations were observed between hormone levels and sexual functioning after correction, underscoring the multifactorial nature of opioid-related sexual health problems.

In the present study, sexual dysfunction was universal, with all participants reporting impairment in at least one domain. The prevalence exceeded international estimates (14-92%) and was comparable with Indian studies (53-92%)[5,7,21-24]. The high prevalence may be attributed to severity of opioid dependence, as indicated by high LDQ scores. Premature ejaculation reported by 72 per cent of participants, seen mainly during abstinence attempt or reduction in heroin use, maintaining or further increasing the relapse risk to heroin use[35].

The hormonal findings in our study differed from the classical opioid-endocrine pattern. Most of the earlier studies on heroin users restricted hormonal assays to testosterone and prolactin levels and typically reported group averages rather than proportions outside reference ranges. In contrast, we found frequent abnormalities across several hormones, including GnRH, prolactin, and DHEAS, while testosterone was largely normal.

At the hypothalamic level, opioids typically suppress pulsatile GnRH release, disrupting the HPG axis[36,37]. Yet, more than half of our participants had elevated GnRH. This requires cautious interpretation, as a single sample may not reliably capture pulsatile activity. One possible explanation is the short-acting nature of heroin, which produces alternating states of intoxication and early withdrawal. These rapid fluctuations may cause cycles of suppression followed by rebound activation of hypothalamic pathways, leading to apparently elevated GnRH at the time of sampling[17,38]. Finally, as GnRH assays are not routinely performed at our centre, measurement variability cannot be excluded.

At the pituitary level, LH and FSH were within the reference range in the vast majority of participants. This is consistent with prior work showing that opioids exert stronger suppressive effects at the hypothalamic level than at the pituitary[36,39]. Unlike the hyperprolactinemia frequently reported in opioid-maintained populations[4,18], the largely normal prolactin profile in our cohort may reflect the lower suppressive potential of short-acting heroin compared to long-acting opioids (such as methadone and buprenorphine), unknown purity, as well as the relative low sensitivity of the pituitary to its effects compared to the hypothalamus[36,39].

At the gonadal level, most had testosterone values within normal limits. Although opioid-induced hypogonadism is well documented in methadone-maintained populations[17,36], findings among heroin users are less consistent[16,38]. The relatively preserved testosterone profile may also reflect the short-acting nature of heroin. At the adrenal level, nearly half of the participants had subnormal DHEAS levels. Evidence on opioid-related suppression of adrenal androgens is limited, though chronic opioid exposure has been associated with HPA axis disruption[37]. These findings suggest that opioid effects on the HPG axis are not strictly linear but involve complex, fluctuating interactions across regulatory levels. This may explain why classical patterns such as uniform hypogonadism

or hyperprolactinemia were not consistently observed in our study.

Findings of exploratory hierarchical regression analyses suggest that, in this cohort, demographic and psychosocial determinants outweighed hormonal influences in explaining variability in sexual function. Although group-level hormonal abnormalities were observed, their lack of independent associations with sexual function implies that opioid-related endocrine disruption may be insufficient on its own to account for the high prevalence of dysfunction. Instead, sexual dysfunction appears multifactorial, reflecting complex interactions between social, behavioural, psychological, and biological factors.

Though psychological distress is a recognised factor in sexual dysfunction, in this cohort, DASS scores indicated minimal symptoms, suggesting other mechanisms were more prominent[40]. Vascular factors are particularly relevant, as nearly 90 per cent of participants were daily tobacco users with moderate-to-high dependence[41]. Relational and social factors also warrant consideration. The paradoxical finding that most married men described themselves as 'very happy' in their marriages while also reporting high rates of IPV (81%) reflects complex cultural dynamics. In some contexts, marital satisfaction may be equated with relationship stability or continued cohabitation despite violence, reflecting normalisation of aggression or social desirability bias[42]. Such dynamics may affect both how sexual health is reported and the quality of sexual relationships, thereby contributing to dysfunction. Comprehensive care should therefore extend beyond hormonal testing to include interventions addressing tobacco use, relationship health, and psychological well-being.

This study has several strengths. It is the first from India to systematically evaluate sexual functioning and a broad panel of sex hormones among untreated men with OD using heroin, filling an important evidence gap. Beyond testosterone and prolactin, we assessed GnRH, LH, FSH, SHBG, and DHEAS, providing a more comprehensive view of the HPG and HPA axes. Methodological rigor was ensured through consecutive sampling, which minimised selection bias[43]. Inclusion of psychosocial measures such as IPV, marital satisfaction, tobacco use, and psychological distress allowed a holistic evaluation of contributors to dysfunction.

Limitations included a cross-sectional design, hormonal assays only at a single time point, and recruitment restriction to sexually active men. Our findings suggest that sexual dysfunction among men with opioid dependence should be understood as a multifactorial problem, driven more by social, relational, and psychological determinants than by hormonal changes. Although hormonal abnormalities were common, they did not explain the dysfunction observed in this population. These results highlight the need for clinicians to move beyond laboratory testing and to routinely address sexual health concerns in individuals with opioid dependence. Integrating psychosocial support and relational interventions alongside biological monitoring, when feasible, may improve quality of life and strengthen engagement with treatment.

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For correspondence: Dr Ravindra Rao, National Drug Dependence Treatment Centre, All India Institute of Medical Sciences, New Delhi110 029, India
e-mail: drrvrao@gmail.com