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Theme: Viral Hepatitis and Addictive Disorders

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- Magnitude of viral hepatitis in substance use disorder
- Prevention of viral hepatitis
- National Viral Hepatitis Control Program

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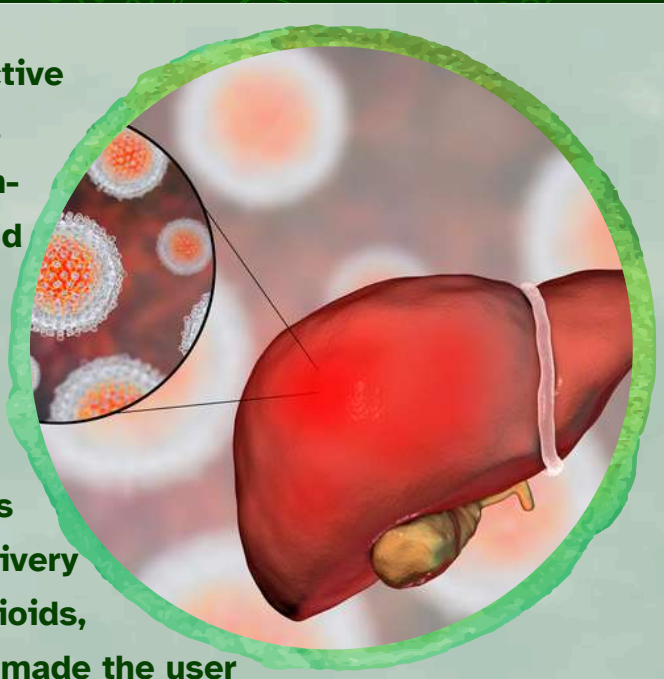
Editorial

Viral Hepatitis: A growing challenge to addictive disorders and their management

Ravindra Rao, Preethy Kathiresan



The association of infectious disease with addictive disorders is not new. Lack of adequate nutrition, poor socio-economic conditions, poor living standards, etc., make the individual using alcohol and drugs vulnerable to various infectious diseases. Tuberculosis was, perhaps, the most notorious of the lot since early times (and, unfortunately, continues to be even today). The introduction of hypodermic needles and syringes in 1853 and its subsequent use for illicit drug use made the delivery of some psychoactive substances, especially opioids, more efficient and addictive. However, this also made the user highly susceptible to infections that are spread through sharing of injecting paraphernalia. HIV is, perhaps, the best-known disease spread with this route. Though HIV has been reduced in the general population in many countries, including in India, HIV prevalence continues to be high among people who inject drugs (PWID) (1). Another infectious disease that is highly prevalent in addictive disorders, especially among PWID, is viral hepatitis, especially, Hepatitis C.

There are five main strains of hepatitis virus, namely, A, B, C, D and E. While hepatitis A and E viruses are predominantly transmitted by faecooral route, hepatitis B, C, and D viruses are transmitted by parenteral (blood-borne) route, sexual route and perinatal route (from infected mother to foetus). HBV and HCV are particularly significant as they cause chronic disease in millions of people worldwide and are the leading causes of liver cirrhosis, hepatocellular carcinoma, and consequently, mortality, due to viral hepatitis. As per the World Drug Report, 2023, between 2010 to 2019, there has been a 13 percent increase in the number of pre-mature deaths and number of healthy years lost due to disability caused by HCV infection among PWID. Once a person is infected with HCV, the disease can manifest in different ways. Most acute HCV infections are asymptomatic; around 30% individuals who are infected with HCV spontaneously clear the virus within six months even without treatment. The remaining 70% develop

chronic HCV infection, if not treated, and around 15% to 30% can develop cirrhosis within 20 years that can further progress on to liver failure or hepatocellular carcinoma.

It is interesting to note that even though the routes of transmission for HCV and HIV are similar, HCV is more prevalent among PWID. There are multiple factors responsible for this difference including the ability of HCV to remain stable outside the human body for longer periods, and to spread with a smaller quantity of blood that is present on the injection paraphernalia. Hepatitis-C virus survives in injection paraphernalia for longer period than HIV (2,3). Similarly, the critical level of needle sharing with injecting partners, below which total infections would drop to minimal levels, is much lower for HCV than for HIV, meaning that greater efforts to reduce injection sharing would be required for HCV than for HIV (4). The high transmissibility of HCV is very much reflected in the high prevalence of HCV among PWID. The first write-up on the prevalence of hepatitis among people with SUD, titled “Viral hepatitis: how big is the problem (and why so big) in substance use disorder?” by Drs Achra and Seth help us understand the gravity of the situation.

While the transmissibility of HCV is much higher than HIV, there are some silver linings with regards to HCV. Firstly, as mentioned above, almost one-third of infected individuals clear HCV spontaneously. Second, and most importantly, there is a cure available for HCV. Earlier, anti-HCV treatment predominantly involved interferons, which were not only expensive, but were also not fully effective and were poorly tolerated. The advent of directly acting antivirals (DAAVs), especially sofosbuvir, revolutionised the treatment of HCV. Currently, HCV treatment has a cure rate of up to 95%. Till recently, sofosbuvir was out of reach of the pockets of most individuals and national programmes. The civil society has played an important role in making HCV treatment affordable and accessible. With multipronged efforts, HCV treatment is now affordable and is available free-of-cost under the National programme to combat viral hepatitis.

Despite these advancements, we still have not been able to eliminate HCV infection; the rates of HCV among PWID continue to remain high (5). One major reason for the same could be the fact that the reach of the program to PWID is still inadequate.

For example, a study from India showed that only a fraction of PWID with HCV seropositivity were aware about their HCV status, and still lesser proportion had seen a doctor and had taken treatment for HCV (6). Prevention of HCV transmission can help in reducing the burden of HCV and associated morbidity and mortality. Since the routes of transmission of HCV and HIV are similar, the same harm reduction strategies applied for HIV can be used to prevent HCV transmission. Or can it be? Whether such strategies help to prevent HCV and whether there is a need to scale up harm reduction measures has been brought out in the article by Drs Parmar and Singh titled "Prevention of viral hepatitis in addictive disorders: are the HIV prevention tools equally effective?".

In 2016, The World Health Assembly adopted a resolution to eliminate viral hepatitis by 2030. In the same year, the World Health Organization (WHO) published the Global Health Sector Strategy on Viral Hepatitis to achieve this goal. A recent report on global hepatitis status by the WHO in 2024 noted that the world is far from achieving the goal to eliminate viral hepatitis by 2030, and that effective implementation at this stage would still reduce the burden due to viral hepatitis significantly (7). The report also says that investing in viral hepatitis prevention and care programmes is cost effective – there is a return of 2–3 USD for every USD invested. The National Viral Hepatitis Control Programme (NVHCP) launched by India has made anti-HCV treatment to patients free of cost. The write-up by Dr. Kabra and colleagues on NVHCP titled "National Viral Hepatitis Control Programme" gives more insight into this landmark programme which promises to bring about a major change in the management of Hepatitis C in our country.

We hope that the current issue, by highlighting the different aspects of the HCV and its relationship with SUD, especially among PWID, will sensitise the readers to this burning topic that is important to bring about difference in the lives of people suffering from the same.

We have two other important write-ups in this issue. On our request, Drs Tripathi and Tiwari have covered the report of the International Narcotics Control Board (INCB) that was released in March 2024. Another write-up, on our request, is from Prof. Atul Ambekar, the society's Secretary General, penning his experience attending the

meeting of the Commission on Narcotic Drugs (CND) in March 2024. We look forward to receiving your feedback on this issue and suggestions for future topics. You can write to us at apsinewsbuzz@gmail.com

Happy reading!

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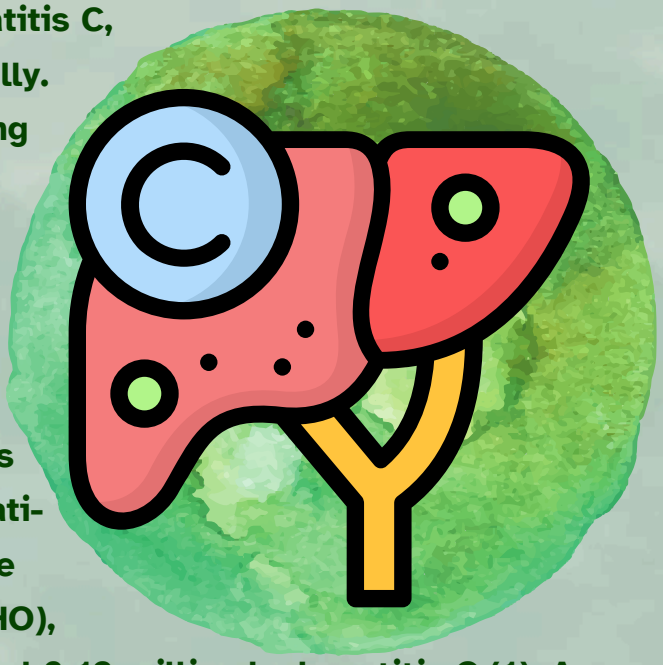
THEMATIC ARTICLES

Viral Hepatitis: How Big Is the Problem (And Why So Big) In Addictive Disorders?

Shalini Singh, Newfight Seth



Viral hepatitis, particularly Hepatitis B and Hepatitis C, presents significant public health concern globally. There are five different types of hepatitis-causing viruses: A, B, C, D, and E. Hepatitis A and E are spread by contaminated water and food. Hepatitis B is transmitted by blood and other bodily fluids and has affected 296 million people till now. Hepatitis C is spread by blood-to-blood contact such as unsafe injection practices. It has affected 58 million people to date. Overall, hepatitis has affected around 350 million people in the world. As per the World Health Organisation (WHO), 40 million Indians are affected by hepatitis B and 6-12 million by hepatitis C (1). As per Indian data, the seroprevalence of hepatitis B and C are 0.95% and 0.32% respectively (2).

This write-up aims to explore the prevalence of Hepatitis-B Virus (HBV) and Hepatitis-C Virus (HCV) infection among individuals with substance use in India with a focus on people who inject drugs (PWID), the reasons behind the heightened prevalence in PWIDs, and the unique consequences of hepatitis in populations with substance use disorder (SUD) compared to the general population.

Prevalence of viral hepatitis in SUD, especially PWID

Injecting drug use is one of the most common causes of HBV and HCV infection among substance users. Every third death due to HCV is attributable to injecting drug use. Globally, the HCV prevalence is estimated to be 48 – 52% and HBV is 7.9 – 8.4% among PWID. It is also estimated that 82% PWIDs with HIV also have HCV (3). A closer look at specific regions of the world shows that there is consistently elevated rate of HBV and HCV infection among PWIDs in the Middle East and North Africa region. Half of PWIDs in the Middle East and North Africa have ever been infected with HCV (4). In Europe, the prevalence of HCV and HBV infection is especially high in the Eastern Europe. Overall, 44.8% PWIDs in Europe are anti-HCV antibody positive

and 2.6% are HBV antigen positive (5). Another study also found that HCV is most prevalent in the eastern Mediterranean region and HBV in the western Pacific and African regions (6).

There is high prevalence of HBV and HCV infection among substance users, particularly PWIDs, in India as well. Studies conducted in various regions of India consistently report elevated rates of HBV and HCV infection among PWIDs. The prevalence of HCV among PWIDs in India ranges from 20% to 90%, with pockets of very high seroprevalence. These rates significantly surpass rates observed in the general population and are comparable to rates reported from western studies (40-90%). (7) Similarly, HBV prevalence among PWIDs in India is substantially high compared to the general population, although data variability exists across different regions.

As per National AIDS Control Organisation (NACO), unsafe injection practices have led to 21 million hepatitis B and 2 million Hepatitis C infections in India. However, there is a lack of national data on viral hepatitis specifically due to injecting drug use. A multi-city study found that the prevalence of HCV is 37.2% among PWIDs (8). Apart from this, few states have published data regarding the prevalence of viral hepatitis in PWIDs. In Delhi, the overall prevalence of HCV and HBV among IDUs visiting drop-in centres is 53.7% and 9.7% respectively. Around 19 % had HIV and HCV coinfection. In Punjab, the prevalence of anti-HCV antibodies was found to be 49%, out of whom, 33% had HIV as coinfection. In Chennai, in a study among treatment seeking population, the prevalence of anti-HCV antibodies was 55%. The median HCV RNA level among those with detectable HCV RNA was 1.24 million IU/ml. Ten percent had hepatic fibrosis due to HCV infection (9,10). Among HIV-infected PWID, the prevalence of coinfection with anti-HCV and hepatitis B surface antigen/anti-HCV was 86% and 9.2% respectively in the city (11). Data from a specialised addiction treatment services setting in Himachal Pradesh shows that the frequencies of HBsAg, anti-HBs, and anti-HCV antibody among PWID were 2.6%, 38.3%, and 9.4% respectively (12). Around 16% PWIDs in Manipur were found to have HBV infection. Among them, 44% had HCV coinfection. Fifteen percent of these viral infections (HBV + HCV) had hepatocellular carcinoma (13).

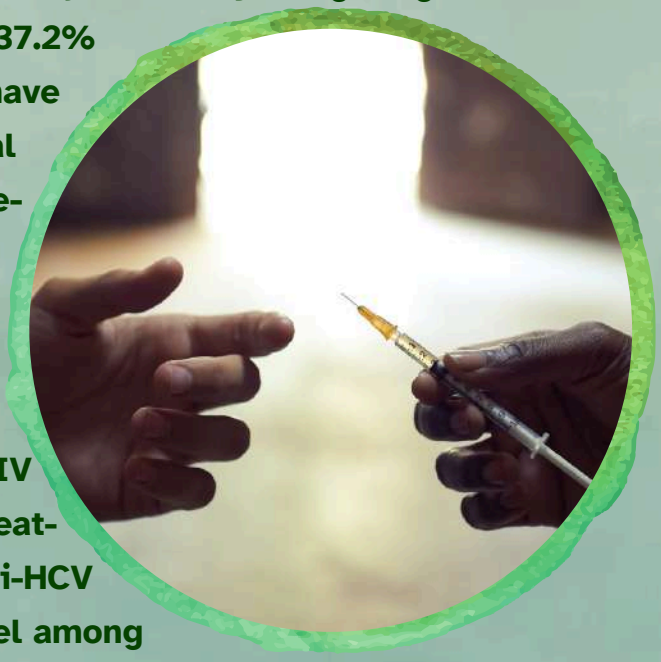


Table 1 outlines the rates of HBV and HCV infection in PWIDs as reported in studies on Indian population. As we can see, there is a huge variation in the reported prevalence of HCV among PWID across different states in our country, which could be due to the difference in the baseline prevalence of HCV in the general population in that region, difference in the study population as well as methodological differences. Despite the variation across studies and regions, it is pertinent to note that the majority of Indian studies have shown a very high prevalence of HCV infection among PWID – nearly 50%.

Table no.1- Prevalence of HBV and HCV among PWIDs in India

Author and year	Setting	State/Cities	HCV prevalence among PWID	HBV prevalence among PWID
Solomon et al., 2015	Community	15 cities across India	37.2%	Data Not Available (NA)
Mahajan et al., 2016	Specialised addiction treatment services	Punjab	38.1%	Data NA
Panda et al., 2014	Targeted intervention settings	Punjab	49%	Data NA
Mehta et al., 2010	NGOs with special services for PWID	Chennai	55%	Data NA
Verma et al., 2020	Specialised addiction treatment services	Himachal Pradesh	9.4%	2.6%
Saraswati et al., 2015	Drop-in Centres	Delhi	53.7%	9.7%

Mahanta et al., 2009		Mizoram and Nagaland	47.8%	3.85%
Wani et al., 2021	Drug treatment clinic in a tertiary care hospital	Kashmir	10%	3.5%

Reasons for high prevalence among PWID

Globally there is a lack of data on hepatitis among substance users specifically in lower and middle-income countries because of the stigma associated with drug use. As per the available data, individuals with longer duration of injecting, younger people, and women have a higher risk of hepatitis among drug users. Hepatitis C is more prevalent than hepatitis B as the former becomes chronic in 75-85% and the latter becomes chronic in only 5% of cases (12). Drug use impairs judgment which causes unsafe injection practices and high risk sexual behavior which further increases the spread of infection. Also, HCV can spread to 20 others within three years among substance users, accelerating the spread even further (14). Additionally, due to the stigma of drug use, treatment of these comorbidities is overlooked.

Besides these, there are several factors that contribute to the heightened prevalence of HBV and HCV among PWID in India:

1) **Lack of Harm Reduction Measures: The primary mode of transmission for HBV and HCV among PWID is through the sharing of contaminated injection equipment, including needles and syringes, facilitating the rapid spread of these viruses within the injecting drug-using community. Despite a nationwide effort to increase accessibility, there is still only a limited availability and accessibility of harm reduction interventions, such as needle exchange programs and opioid substitution therapy, which contributes to ongoing transmission of viral hepatitis among PWID.**

2) **Socioeconomic Factors: PWID often face socioeconomic challenges, including poverty, homelessness, lack of awareness about impact of high risk behaviours, which increase their vulnerability to viral hepatitis infections.**

3) **Lack of treatment services: The high prevalence of HCV infection and HIV-HCV co-infection in PWIDs coupled with paucity of services for screening, diagnosis and management of HCV infection has contributed to the high disease burden of viral hepatitis in this population.**

4) Co-infection with HIV: The co-occurrence of HIV infection among PWID further exacerbates the risk of HBV and HCV transmission due to shared risk behaviours and overlapping routes of transmission.

Consequences of Hepatitis in SUD Populations

The consequences of hepatitis, particularly HCV, in SUD populations extend beyond the traditional health impacts observed in the general population.

1) Accelerated Disease Progression: Individuals with SUD, especially those who inject drugs, are more likely to experience rapid progression of liver disease following HCV infection, leading to increased morbidity and mortality.

2) Barriers to Care: Stigmatization and discrimination associated with substance use may deter individuals from seeking timely healthcare services for hepatitis diagnosis and treatment, exacerbating disease progression.

3) Complex Treatment Landscape: The management of viral hepatitis in SUD populations is complicated by challenges such as ongoing substance use, adherence to treatment regimens, and potential drug interactions with medications used for hepatitis treatment.

In conclusion, the prevalence of viral hepatitis, particularly HBV and HCV, is disproportionately high among substance users in India, notably among PWID. The heightened prevalence can be attributed to injection practices, socioeconomic factors, and limited harm reduction measures. Furthermore, the consequences of hepatitis in SUD populations extend beyond those observed in the general population, highlighting the need for targeted interventions and comprehensive healthcare approaches to address the unique needs of substance users affected by viral hepatitis.

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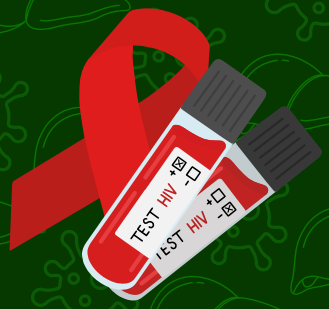
Prevention of Viral Hepatitis in Addictive Disorders: Are the HIV Prevention Tools Equally Effective?



Arpit Parmar, Gaurav Kumar Singh

Introduction

Harm reduction is a key public health intervention that is highly effective in reducing and mitigating harms related to injecting drug use, especially HIV, at the individual and community levels. As per the consolidated guidelines on HIV, viral hepatitis, and STI prevention, diagnosis, treatment, and care for key populations released by the WHO in 2022, PWID is one of the five key populations with respect to blood-borne infections (1). The document defines harm reduction as policies aimed at preventing major individual and public health harms of drug use, such as HIV, hepatitis B and C, and opioid overdose, without necessarily quitting drugs. The harm reduction package includes Needle Syringe Programs (NSPs), Opioid Agonist Maintenance Treatment (OAMT), and naloxone for overdose management, among many other interventions. Among these, OAMT and NSPs are found to be most effective in preventing the HCV and HIV transmission associated with injecting practices. It has been seen that PWID prioritize access to these harm-reduction services over other health interventions (1).

Evidence of effectiveness of harm reduction interventions

A 2014 review of reviews assessed the effectiveness of such interventions in preventing HCV and HIV in PWID (2). Their review of 12 core and 13 supplementary reviews inferred that there is little review-level evidence for the effectiveness of OAMT and NSP in preventing HCV acquisition among PWID. At the same time, they were robustly effective in preventing HIV and reducing other injecting risk behaviors. NSPs decrease HIV transmission by 48% (a moderate effect), while OAMT reduces HIV transmission by 54% (a strong effect).

On the other hand, UK data suggested that OAMT and NSP (≥100% coverage) are both associated with a reduction in HCV acquisition risk by 50% individually and in combination by 80% (3). Effective management of PWID requires receipt of high

doses of agonist management and is particularly important for reducing HCV infection and related harms.

A recent meta-analysis and Cochrane review provided useful information on the effectiveness of these interventions in HCV prevention (4). As per the study, OAMT reduces the risk of HCV transmission and is further strengthened by combination with NSP. For example, current OAMT enrolment was associated with a 50% reduction in HCV acquisition risk. High coverage of NSP (as defined by regular attendance in NSP or ≥100% coverage) was associated with a 56% reduction in the HCV acquisition. On the other hand, combined OAMT and NSPs were associated with a 74% reduction. The meta-analysis emphasizes the need for higher coverage of NSP and OAMT.

Interestingly, the decline in HCV incidence in Scotland has been attributed to the scale-up of OAMT and NSP (5). Some other modeling studies report that scaling up these interventions may reduce HCV transmission, but the reduction in prevalence may be modest and require long-term sustained coverage (6). A pooled analysis of three trials reported that comprehensive OAMT/NSP led to a 41% lower HIV acquisition and 76% lower HCV acquisition risk (7). Though the effectiveness of NSP in reducing HIV acquisition and transmission is graded as "sufficient" in a recent systematic review of systematic reviews, it is graded as "inconsistent" for the transmission of HCV (8). This may be attributed to differences in NSP interventions, their implementation, and geographical differences. The study further emphasized the role of comprehensive harm reduction interventions at the structural level that integrates multiple interventions along with NSP, including OAMT. Some studies have also focused on different aspects of NSP provision and its impact on HCV and HIV-related outcomes. One initial review reported no difference in HCV prevalence when various sources of NSP (such as van-based NSP, fixed-site NSP, and pharmacies)were compared (10). Further, the NSP setting does not seem to impact the risky behaviors associated with injecting practices.

Thus, we can infer that NSP and OAMT, particularly in combination, are effective in reducing both HIV and HCV transmission among PWID (8). Hence, the WHO and UNODC emphasize the need to integrate these harm reduction interventions with simplified service delivery in a public health approach that also includes HCV

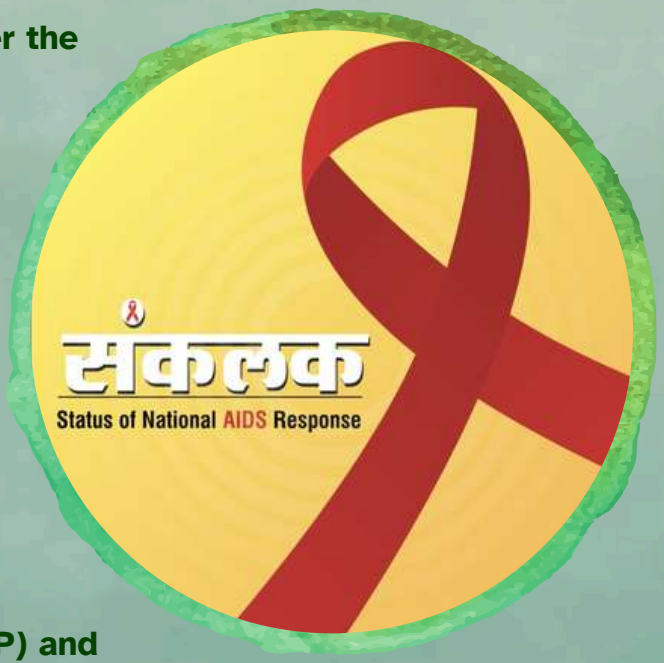
testing, Anti-virals (DAAs) (9).

Coverage of harm reduction interventions

Despite the evidence for its effectiveness, the abysmal coverage of these interventions, especially in low and middle-income countries, remains a major barrier. WHO-recommended targets for harm reduction interventions include the distribution of more than 300 needles and syringes per PWID per year and OAMT provision for more than 40 people per 100 PWID per year. A recent systematic review to assess global, regional, and country-level coverage of these interventions among PWID reported that the coverage with these interventions varied widely but remained low for most of the included countries (11). Some NSP and OAMT services were available in 93 and 86 countries, respectively. Around 33 needles and syringes are distributed per PWID per year, while only 16 PWID are recipients of OAMT globally. Thus, the coverage of HCV prevention/harm reduction interventions for PWID remains poor in most countries and, therefore, is unlikely to be effective in preventing HCV transmission. Scaling up the harm minimization interventions remains a priority for preventing HCV acquisition among PWID.

Coverage of harm reduction interventions in India

In India, these interventions are provided under the National AIDS Control Program (NACP) as HIV prevention tools. The National Viral Hepatitis Control Program also recommends harm reduction interventions for the prevention and management of hepatitis B and C among key populations, including PWID. Although these interventions have been provided for around two decades in India, their coverage remains poor. As per the Sankalak: Status of National AIDS and STD Response 2023, the coverage of targeted intervention projects (that provide NSP) and OAMT services for 2022-23 is around 2.07 lakh and 44,553 PWID, respectively (12). This is abysmally low, considering the huge numbers of PWID in India (approximately 8.5 lakhs as per the recent national survey). The current coverage of OAMT in India is three per 100 PWID (four per 100 PWID who primarily inject opioids), while the coverage for NSP is around 34 needles and syringes per PWID per year (11). This is far below the WHO-recommended coverage cut-offs for harm reduction interventions.



Conclusion

To conclude, the harm reduction interventions, OAMT and NSP, are both effective in reducing viral hepatitis transmission among PWID. These interventions are most effective when used together. However, their coverage is abysmally low in most countries, including in India. This highlights the importance of scaling up these harm reduction interventions for PWID. Further research is needed to identify the most effective ways and service delivery models for the implementation of these interventions in countries like India.

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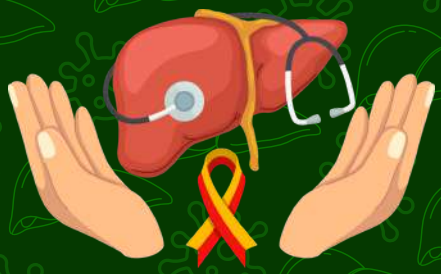
National Viral Hepatitis Control Program

Sandhya Kabra, Preeti Madan, Partha Rakshit, Hema Gogia



Background

Viral hepatitis is a major public health challenge worldwide, including in India. As per the WHO Global Hepatitis report 2024, around 254 million people live with hepatitis B and 50 million with hepatitis C in 2022 (data from 187 countries) (1). As per 2023 HIV Sentinel Surveillance Plus report, the national seroprevalence for hepatitis B and hepatitis C was found to be 0.85% (95% CI 0.85-0.86) and 0.29% (95% CI 0.29-0.30) respectively. The seroprevalence of hepatitis B was highest in Bihar followed by Mizoram, Delhi, Madhya Pradesh & Meghalaya. The seroprevalence of hepatitis C was highest in Mizoram followed by Punjab, Haryana, Uttarakhand, Uttar Pradesh, Karnataka, and Delhi.

The National Viral Hepatitis Control Program was launched in 2018 under National Health Mission with the aim to combat hepatitis and eliminate hepatitis C by 2030 and reduce morbidity and mortality due to other types of viral hepatitis in line with Sustainable Development Goal (SDG) 3.3. Under the program, free diagnostics and drugs are being made available to all in need, not only for treatment of hepatitis C but also for management of hepatitis B. The key strategies adopted under the program include preventive, promotive and curative interventions with the focus on awareness generation, increasing access, capacity building of all concerned stakeholders, promoting diagnosis and providing treatment for viral hepatitis across the country in sync with the universal health coverage for all.

The program through the National Health Mission has formulated strategies utilizing the existing resources in health systems including infrastructure, manpower and established mechanisms of diagnostics and treatment services optimizing equitable access to services with financial efficiencies.

Implementation of NVHCP

- At the national level, a national programme steering committee headed by the

Secretary, Health and Family Welfare, Govt. of India provides guidance to and monitors the implementation of the programme. The National Viral Hepatitis Control Management Unit (NVHMU) established within the National Health Mission is responsible for the implementation of the activities of the programme. The NVHMU is supported by the state and district viral hepatitis control management unit in each state and union territory. Each state has a designated nodal officer who oversees the implementation of the programme in the respective state. The list of nodal officers is available at https://nvhcp.mohfw.gov.in/Landingpage/List_of_Nodal_officers

- National guidelines for diagnosis and management of viral hepatitis have also been developed and released so as to ensure standardization of the laboratory and treatment protocols. The guidelines are as mentioned below and are available on the NVHCP website i.e. www.nvhcp.mohfw.gov.in

  1) National Guidelines for Diagnosis & Management of Viral Hepatitis
  2) National Laboratory Guidelines for Testing of Viral Hepatitis
  3) National Viral Hepatitis Control Program Operational Guidelines
  4) Technical Guidelines for Diagnosis & management of Hepatitis B

- A call centre (1800-11-6666) has also been established for responding to queries associated with viral hepatitis and services being offered under the program.

- The services for the treatment are delivered through designated treatment sites located within existing health facilities such as district hospitals and medical colleges/institutions. Referral centres named as Model hepatitis treatment centres (MTC) located in tertiary level healthcare facilities have also been established in all states/UTs to act as referral units for management of complicated cases as well as special cases such as pediatric patients, patients with treatment failure, etc.

- The Program has established 978 treatment sites in 711 districts across the country. It has screened 10.34 crore individuals for hepatitis B & C and provided treatment access to 3.3 lakhs patients till March 2024 since its inception.

- The program has integrated with national programs/schemes and other ministries for efficient utilization of resources. Some examples to showcase this include

a. RMNCAH+N (Reproductive, Maternal, Newborn, Child, Adolescent Health and Nutrition) to ensure that all pregnant women are screened for biomarker of hepatitis B (HBsAg) during the first antenatal visit for HBV infection. HBsAg-screened positive pregnant woman are categorized as high-risk pregnancy and referred to designated healthcare facilities where the newborn of these women can get Hepatitis B immunoglobulin (HBIG) along with birth dose of Hepatitis B vaccine. The screened positive pregnant woman is also counselled for getting her first-degree relatives screened for HBV infection and she is referred to designated treatment centres for further management under NVHCP.

b. National AIDS Control Program to ensure that all high-risk groups listed under the program be screened for hepatitis B and hepatitis C so that those screened positive for the hepatitis B/C to be linked to treatment centres under NVHCP. Those screened negative are vaccinated against Hepatitis B at the healthcare facility through the health systems.

People who inject drugs (PWID) and NVHCP

NVHCP is committed to address high prevalence of hepatitis C among PWID. The programme intends to integrate with substance use disorder (SUD) program for extending services of prevention, diagnosis and treatment/management to those in need.

Conclusion

Elimination of viral hepatitis has been accorded importance at the highest level by its incorporation in the sustainable development goal. Accordingly, the Government of India has set up a separate national programme i.e. National Viral Hepatitis Control Programme, to address viral hepatitis. In a short span of time, the programme has strengthened existing systems/healthcare facilities for identification and management of viral hepatitis. The efforts have now begun to bear fruit as can be seen from the increasing number of tests conducted and treatment provided. However, the programme cannot succeed unless high-risk groups including PWID get greater access to services for management of viral hepatitis. NVHCP is now focusing its attention on PWIDs through coordination and linkage with existing programmes and activities that reach out to this group.

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WHAT'S NEW

Attending Commission on Narcotic Drugs (CND) meeting at Vienna: An Experiential Account

Atul Ambekar

In March every year, all the UN member countries gather in Vienna, Austria (the headquarter of UNODC), for the meeting ('session') of Commission on Narcotic Drugs (CND). CND is the central drug policymaking body of the UN. The national delegations usually comprise of a mix of officials representing the drug supply control sector, the drug demand and harm reduction sector as well as diplomats.

I have had the privilege of being a part of Indian delegations at CND since 2020, on behalf of the Ministry of Health and Family Welfare. This year, the 67th session of CND was special since this included the 'high level segment': meeting of higher-level representatives to review the mid-term progress of the 'ministerial declaration' (2019-2029) – a 10-year declaration by the global community to address the drug problem. Our 10-member delegation was headed by the Additional Secretary, Revenue, Ministry of Finance. Other departments and agencies included representatives of departments of Home Affairs, Social Justice and Empowerment, Narcotic Control Bureau (NCB), Central Bureau of Narcotics (CBN), Pharmaceuticals, Chemicals, and the representatives from the Indian mission in Vienna.

The purpose of the CND sessions is to exchange expertise, experiences, and information on drug-related matters and to develop a coordinated response to the drug situation. The discussions are conducted in a rather formal and structured manner. The agenda includes a review of the progress made in the work of various UN agencies (such as UNODC, WHO and INCB) tasked with specific mandates for international drug control. During the discussion, each delegation gets the opportunity to address the house which is usually in the form of reading a statement (making an 'intervention'). I made two statements on behalf of India on (a) Challenges posed by the New Psychoactive Substances (NPS) and (b) Harm reduction interventions by India to address HIV among People Who Inject Drugs. Another major agenda during the CND

sessions is decision about bringing newer substances into the list of internationally scheduled narcotic drugs or psychotropic substances. Every year, after conducting a thorough review, the Expert Committee on Drug Dependence of WHO recommends scheduling of some substances as narcotic or psychotropic. The CND member states, through a process of voting, either accept or reject the WHO recommendations.

While the discussion on the primary CND agenda (plenary session) takes place in the main hall, simultaneously in another hall ('Committee of the Whole' or COW) another discussion takes place on the text of CND resolutions. This discussion is very interesting since each and every word in the text is scrutinized by the delegates and after a heated debate, through the so-called "Vienna spirit" the resolutions are agreed usually by consensus, in the plenary on the final day. This year was different and indeed historical. Probably for the first time in many years, one of the CND resolutions by the USA on Overdose Prevention failed to generate consensus. Some countries (Russia and China) continued to oppose inclusion of the term 'Harm Reduction' in the text of the resolution. Notably, while Harm Reduction has been a widely accepted approach by the global scientific community, the CND has traditionally shied away from using this term. On the final day of 67th session the debate on resolutions continued till very late in the evening. With consensus nowhere in sight, the chair had to ask for voting and ultimately with an overwhelming support (38 countries in favor, 2 against and 6 abstentions) the resolution was adopted by the CND. This is indeed historical for two reasons. This breaks the tradition of Vienna spirit and normalizes disagreement. Secondly, this establishes harm reduction as the 'agreed phrase' in CND. Curiously, till a few years ago, the USA delegation used to be a staunch opponent of the phrase 'harm reduction'. The lesson to the world is: with the changing drug situation, wise countries must adopt approaches which are evidence-based and compliant with human rights without being dogmatic.

Contrary to the perception, CND is not just about government diplomats talking to each other. There is space for civil society too. During the breaks between the plenary sessions, multiple 'side-events' are organized in parallel (similar to parallel symposia in our conferences). Such events are typically about 50 minutes long with 3-4 speakers followed by Q&A. Civil society organizations can speak at these side events. Topics of these side events can be anything related to illicit drugs – from supply

control to demand reduction and harm reduction. Incidentally, I had the opportunity to deliver a brief talk in one of the side events in CND 2023 organized by the Government of India (co-sponsored by USA). Besides the side events, another important forum for the NGOs is informal consultations or dialogue of civil society with UN entities like the CND secretariat, INCB, WHO and UNODC. During these dialogues, the NGO representatives get to ask (sometimes uncomfortable) questions to the UN agencies on their activities (or inactivity!) on some specific issue, thus demonstrating an attempt to make the UN system accountable to civil society also (along with their accountability to the national governments).

Apart from these programs at CND, the member states also find opportunities to engage in brief bilateral meetings between the delegates of other countries to discuss the issues of mutual interest related to drug control. This year, our delegation participated in more than a dozen bilateral meetings with other country delegations.

Is CND useful? Questions are sometimes raised about the utility and effectiveness of holding large in-person meetings like CND annually. Personally, I see CND as a valuable opportunity for all the member states to convene and exchange notes on newer developments in drug control. Notably, as a part of preparing for the CND session, all the national governments and more importantly various government departments dealing with illicit drugs are forced to come together, which augurs well for a coordinated response to the drug problem. The fact that subject-matter experts are also included in the CND delegation by the Government of India should be appreciated. It would be even more useful to hold a de-briefing session post-CND and publish its report in the public domain.

Personally, participating in the CND sessions has been a huge learning opportunity as well as a humbling experience for me. One realizes that addiction psychiatry forms a tiny (though not insignificant) part of the response to the global drug problem.

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Report of the International Narcotics Control Board, 2023

Richa Tripathi, Shubhankar Tiwary

The International Narcotics Control Board (INCB) is an independent and quasi-judicial monitoring body for the implementation of the United Nations international drug control conventions. It was established in 1968 in accordance with the single convention on narcotics, 1961. The broad function of INCB is to ensure that adequate supplies of drugs are available for medical and scientific uses, and to identify weaknesses in national and international control systems. The INCB releases its report annually in which it provides information on the global and national situation with regards to drug control. Additionally, it covers one theme related to drug use or control in detail. This year, the *INCB report* was released on March 5, 2024. The thematic area covered this time focuses on the role of internet, including social media, in drug trafficking and use.

In the chapter on the role of internet, the Board noted the opportunities and challenges posed by internet in combating drug use and trafficking. The online platforms can be used to prevent non-medical use of drugs, raise awareness about the harms of drug use and support public health initiatives. However, the internet has also facilitated illegal drug supply. Illicit drug trafficking has been a major concern globally with the use of internet and advancements in newer technologies besides the conventional routes of trafficking in post-covid era. The internet connects potential buyers and sellers across the globe with a large audience base. Use of cryptophones and darknets to procure drugs has become common in youngsters. Drug trade through these crypto-markets are relatively safe and cheaper than the social marketing site and evades detection by law enforcements. There are jurisdictional issues related to internet-facilitated drug trafficking, and offenders can easily move their activities to territories with less intensive law enforcement action. The chapter also mentions various practical tools and online systems that the Board has developed to facilitate international trade and control illicit trafficking.

The report has noted the persistence of disparity between various regions with regards to the consumption of opioid analgesics such as morphine for the treatment of pain. The levels of opioid consumption in North America, Oceania and Western and Central Europe are way higher than other regions in the world. The average levels of consumption reported in 2022 in East and South-East Asia, Central America and the Caribbean, Africa and South Asia were inadequate and are of particular concern. The South Asia region has the lowest consumption of opioids for pain relief. Surprisingly, this imbalance did not stem from a shortage of opiate raw materials. Many opium producing countries such as Australia are growing noscapine-rich opium poppy besides morphine, thebaine and oripavine. The Board has called upon all the stakeholders to improve the existing discrepancy in opioid consumption for pain relief.

The Board has added few new drugs in the list of narcotics and psychotropics in the past year. Similarly, the Board also reported that some chemical groups that could be used as precursors were also included for scheduling. These precursors were related to amphetamine-type stimulants and fentanyl analogues. The report also observed that benzodiazepines, Phenobarbital, methylphenidate and Zolpidem were most traded psychotropics. Phenobarbital is the most heavily manufactured psychotropic in 2022. The Board has also noted limited availability of data on consumption of internationally controlled psychotropic substances for medical and scientific purposes. The licit cultivation, production and utilization of cannabis has followed an upward trend but that of cocaine was reduced.

In its regional overview section, the Board has noted variations in drug use and drug control across region. For example, a reduction in opium poppy cultivation and increased manufacture of methamphetamine was observed in Afghanistan. The manufacture of and trafficking of falsified “captagon” continues to be a serious public health problem in countries of Middle East. A high potent form of cannabis called as “skunk” represents a challenge in Türkiye. The non-medical use of tramadol and high prevalence of HIV among people who inject drugs continues to pose a major threat to public health in the Middle East. Cultivation of cannabis for recreational use has been permitted in many European countries and United States. Several European countries have placed the cannabinoid hexahydrocannabinol (HHC) and its derivatives under national control. A special report released by EMCDDA draws attention to the use of

nitrous oxide as a growing concern for Europe, especially among young people.

With regards to South Asia region to which India belongs, the Board notes high prevalence of opiate users in South Asia, amounting to 39 per cent of the total number of opiate users worldwide. India accounted for 90 per cent of the region's opiate users. Narcoterrorism appears to be an increasing problem in the region, wherein the proceeds of drug trafficking are used to fund terrorism and armed groups. While the production of opium for licit purposes in India is stable, it also continues to be illicitly cultivated, particularly from the north-eastern region of the country. Most heroin found in South Asia appears to have originated from illicit opium produced in Afghanistan. Use of methamphetamine has found to be increasing in India. The country is being exposed to the expansion of methamphetamine trafficking from both South-West and South-East Asia.

The report also has a section in which the continued challenges faced by governments around the world to resume provision of public drug use treatment and rehabilitation services has been noted. The section also mentioned the provision of non-evidence-based treatment in compulsory drug treatment centres as well as in other centres that are supported by the government. The shift in drug use patterns in many regions may also prove challenging for the governments to provide effective treatment. The section concludes with the Board calling upon governments to ensure access to voluntary, evidence-based treatment services, in line with UNODC and WHO International standards for the treatment of drug use disorders.

The last chapter lists 29 recommendations of the Board to governments, the United Nations and other relevant organizations. These recommendations range from use and regulation of internet, adherence to the international drug conventions, avoidance of extrajudicial action taken in the name of drug control, consider abolition of death penalty for drug-related offences, prioritise data collection on drug use, to building capacities in demand reduction activities, and use various online platforms developed by INCB for drug control.

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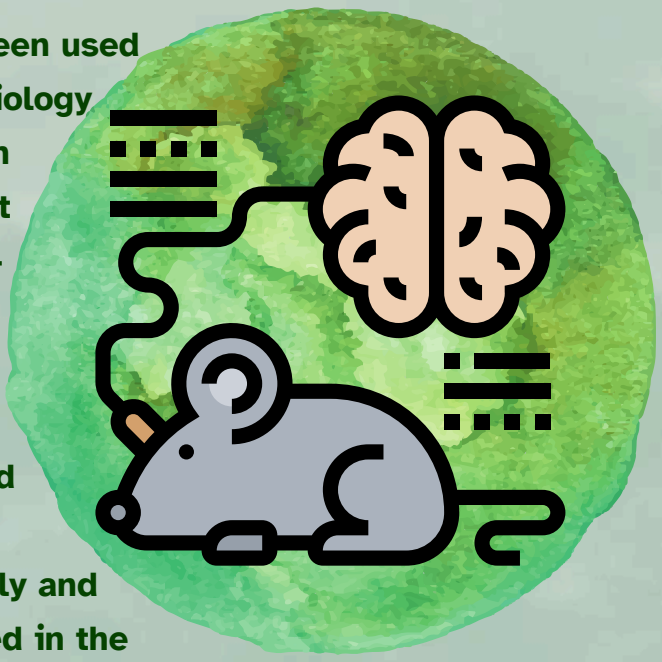
RECENT ADVANCES

Basic Sciences of Addiction

Jayant Mahadevan



There are several new technologies that have been used to investigate the neurocircuitry and synaptic biology of addictive disorders. Optogenetics is one such major technological advance. It is a method that can modulate the activity of cells, such as neurons, using a combination of optical and genetic targeting. It involves the expression of light-sensitive microbial opsins within a genetically-specified population of neurons. This is followed by delivery of light to activate these opsins and thereby modulate the targeted cells in a spatially and temporally defined manner. The changes induced in the targeted cells are then verified using in-vivo techniques and the relationship of these changes to animal behaviour is studied (1).

A study on the neural basis of reward and behavioural reinforcement genetically isolated two populations of dopamine-producing neurons in the ventral tegmental area (VTA) that have distinct projections to the nucleus accumbens (NAc) core and shell. By using optogenetic techniques, it was found that the selective activation of VTA-core projecting neurons promoted initial reward learning, while activation of VTA-shell projecting neurons did not but could drive robust responding in a previously learned instrumental task. The simultaneous activation of VTA-core and VTA-shell neurons further resulted in more robust self-stimulation and the emergence of a real-time place preference, indicating a synergistic action of these distinct dopamine populations. The study provided evidence for the existence of functionally distinct dopamine populations in the VTA that promote motivation and reward association and work together to optimize behavioural reinforcement (2).

Another study evaluated the neural basis of aversive states such as drug withdrawal by activation of mu-opioid receptors (MORs) in the habenula (Hb). It was seen that the optogenetic stimulation of Hb-MOR neurons leads to behavioural avoidance, despair-like behaviour, and increased anxiety levels. Hb-MOR neurons project to both the

interpeduncular nucleus (IPN) and the dorsal raphe nucleus (DRN). Further it was seen that a specific stimulation of Hb-MOR neurons projecting to the IPN induced avoidance behaviour and despair-like behaviour, while stimulation of Hb-MOR neurons projecting to the DRN increases anxiety levels. It was seen that endogenous or exogenous MOR signalling in the Hb, which inhibits Hb-MOR neurons, may alleviate negative affective states through the IPN or DRN pathways. Thus, MOR activity in the Hb has an "aversion-reducing" function and positively regulates hedonic homeostasis. The findings suggest that endogenous opioids may alleviate aversive states by inhibiting Hb-MOR neurons, contributing to hedonic homeostasis and addiction. Thus, we can see that optogenetics help in stimulation of specific neurons and can be helpful in advancing the neuroscience of addiction further (3).

Finally, a translational study which investigated the effects of optogenetic stimulation of specific neurons in the nucleus accumbens on cocaine reinstatement found that high frequency optogenetic stimulation of D2DR-containing neurons in the nucleus accumbens shell attenuated cocaine-primed reinstatement of cocaine seeking in male rats, while high frequency optogenetic stimulation of D1DR-containing neurons in the nucleus accumbens shell did not alter cocaine-primed reinstatement of cocaine seeking in male rats. These effects were not seen in female rats. The study highlights the importance of considering cell type specificity in understanding the mechanisms of DBS in modulating behaviour and supports our previous understanding of how D2 type receptors may reduce drug reward. It also highlights the previously documented sex in response to cocaine (4).

Therefore, optogenetic experiments have confirmed some of the previously established findings related to the neurobiology of addictive disorders and also provided potentially newer avenues for exploration and therapeutics. However, there are certain limitations to this technique use in humans. Since it may involve the use of viral vectors to transduce the target tissue with specific opsins or use of neurosurgery to implant biomedical device to stimulate the transduced opsins, there are risks associated with these techniques. Also, whether these risks would be less than the benefits that optogenetics could offer is again a matter to ponder upon. Optogenetics have been used only in animal studies of addiction till now. Human clinical trials of optogenetics is currently ongoing for retinitis pigmentosa only and even for these studies, the results have not been published yet (5). Hence, till the safety of this

technique in humans is established, it will predominantly be used for addiction research in animal models only.

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Alcohol and Tobacco

Kamini Verma, Aniruddha Basu

E-cigarette (EC) initially introduced in 2005 are defined as electronic forms of heating of nicotine or non-nicotine-based substances with different adjuncts like glycerine, menthol, etc., which, when inhaled, gives the feeling of smoking real tobacco cigarettes (1). Soon after its introduction, e-cigarettes gained popularity among youngsters. The e-cigarette market has seen significant growth, with its global value increasing from $11.73 billion in 2019 to almost $21.4 billion by 2023. In less than a decade, the prevalence of past-month ENDS usage increased from 1.5% to 27.5 % among US high-school students. A meta-analysis done in 2021 with a sample of 3925 youngsters world-wide showed that the prevalence of ENDS use was highest in high-income geographical regions, the pooled prevalence for ever lifetime ENDS use was 17.2%, whereas for current usage, it is 7.8% (2). There is significant variability in the prevalence of ENDS globally by country income status. In India as per GATS survey 2016-2017, 3% of adults in India knew about e-cigarettes while the number who used e-cigarettes was 0.02% and it was mostly confined to urban areas . These findings are possibly due to differences in regulatory context, market availability, and differences in surveillance systems. Based on the World Health Organization and Indian Council of Medical Research recommendations, India imposed a complete ban on EC in 2019 (3). Even though it has been five years since the ban, EC is still being sold in India's grey markets, where marketing is not regulated as per newspaper reports.

In this background, we decided to review a recent phase-three, randomized, controlled trial published in the New England Journal of Medicine. The study by Auer et al, 2024 (4) aspired to assess the safety and efficacy of e-cigarettes in addition to standard care compared to standard care alone in an of e-cigarettes in addition to standard care compared to standard care alone in an open-label, controlled, trial which enrolled adult smokers who had smoked at least five cigarettes per day. The intervention arm received free e-cigarette and e-liquid, counselling, and optional NRT and the control

group received counselling and voucher which they could use for any purpose, including NRT. The primary out-come was biochemically validated abstinence from smoking. A total of 1246 participants underwent randomization, 622 participants were assigned to the intervention group, and 624 to the control group. The percentage of participants with validated continuous abstinence from tobacco smoking was 28.9% in the intervention group and 16.3% in the control group (relative risk, 1.77). Serious adverse events occurred in 25 participants (4.0%) in the intervention group and in 31 (5.0%) in the control group. The study concluded that addition of e-cigarettes to standard smoking cessation counselling resulted in greater abstinence from tobacco use among smokers than smoking-cessation counselling alone. Many of the smokers who abstained from smoking tobacco continued using e-cigarettes. Though the findings are important, there are several limitations. Firstly, this is an open label study which may have influenced the outcomes. In the control group, free nicotine replacement was not provided unlike the intervention group. Only outcome of six months was assessed; the long-term effect of e-cigarettes needs to be assessed in future. The generalizability needs to be tested in our settings particularly whether it can be extrapolated to Indian conditions*. Also, the long term safety as well as harms associated with e-cigarette use is still not well established. This is pertinent to consider since many people who abstained from tobacco smoking still continued e-cigarettes.

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**The ban on e-cigarettes by the Government of India extends to research on these products as well.*

Illicit Drugs

Shinjini Choudhury

Cannabis continues to remain the most prevalent illicit drug used worldwide. Besides the development of cannabis use disorders (CUD), cannabis use can also lead to various other far-reaching adverse effects, both at the individual level and societal level (1). Despite its wide prevalence, there is still a lacuna in the pharmacological treatment option that specifically targets cannabis use disorder. Recent research is exploring new pharmacological agents for management of cannabis use disorder.

"Signal Specific Inhibitors of CB1" – Herald of a new avenue of treatment for cannabis use disorder?

Available orthosteric antagonists or inverse agonists of the cannabinoid type 1 (CB1) receptor inhibit all CB1 receptor-mediated action including normal endocannabinoid function, leading to serious adverse effects, limiting their tolerability and wider applicability. The search for a therapeutic agent with more precise mechanism of action has led to the development of a new pharmacological class of drugs, named as 'signaling-specific inhibitors of the CB1' (CB1-SSi) (2).

CB1-SSi drugs have been developed modelled on the steroid 'pregnenolone' which is released endogenously in response to high concentrations of Tetrahydrocannabinol (THC). Pregnenolone specifically inhibits CB1-mediated changes in MAPK (Mitogen Activated Protein Kinase) phosphorylation and mitochondrial respiration, but not CB1 mediated changes in cAMP (3). As a result, pregnenolone inhibits many of THC's effect without causing behavioural changes. While these effects may appear to favour pregnenolone to be a superior therapeutic agent, its short half-life, low oral bioavailability, and conversion into other active steroids inside the body (leading to serious adverse effects) all prevent it from being a viable treatment option. The CB1-SSi drugs also do not modify CB1-mediated changes in cAMP, ensuring that endocannabinoid function remains unaffected, thereby enhancing its tolerability.

The risk of CB1 receptor inhibitor-mediated precipitation of cannabis withdrawal is also mitigated by this specificity of CB1-SSi.

An ongoing project studying the first CB1-SSi, AEF0117, has yielded promising results in phase 2a trials, while results from the phase 2b trials are expected later this year. The phase 2a trials had a randomised, double-blind, placebo-controlled, crossover study design. The study sample consisted of 29 non-treatment seeking adult volunteers aged 21 to 60 years with CUD. The group was randomised into two ascending-dose cohorts. While one cohort received low oral dose of AEF0017 daily for 5 days (0.06 mg, n = 14), the other group received high oral dose of AEF0117 daily for 5 days (1 mg, n = 15). Both the groups also received placebo, based on randomisation at different time points and the crossover between placebo and drug was 14 days or more. The primary outcome, measured by visual analogue scales, assessed the positive subjective effects of cannabis. AEF0117 was found to significantly reduce cannabis' positive subjective effects by 19% (0.06 mg) and 38% (1 mg) compared to placebo ($p < 0.04$). There was also reduction in cannabis self-administration ($p < 0.05$), an important secondary outcome, without any adverse effects or precipitated withdrawal (2). If the ongoing phase-2b and subsequently phase-3 trials continue to support such findings, this group of drugs could potentially change the treatment of cannabis use disorder and help the patients suffering from the same.

While researchers are trying to advance the treatment of cannabis use disorder, a new psychoactive compound related to cannabis is posing a threat to the public health.

Delta-8-Tetrahydrocannabinol (delta-8-THC) - An emerging public health threat?

Delta-8-THC, a positional isomer of delta-9-THC, is one of the hundreds of cannabinoid products produced naturally by cannabis plant. It is present in very low amount naturally, in contrast to Delta-9-THC, which is the most abundant cannabinoid in the cannabis plant. It is largely an unregulated psychoactive compound and first appeared in the US markets in 2010s. Following the enactment of the USA's Farm Bill of 2018, 2018, hemp was removed from the purview of the Controlled Substances Act (4). Soon, reports of adverse effects and intoxication due to use of Delta-8-THC products, requiring hospitalisation began to emerge in USA. Some of these adverse events included hallucinations, tremors, vomiting, anxiety, dizziness, confusion, etc.

Between 1st December 2020 and 28th February 2022, at least 104 reports of adverse events were documented by the FDA due to the use of Delta-8-THC products. During the same period, the National Poison Control Centres of USA reported 2362 cases of exposure, 80% of it being unintentional among paediatric cases. Besides the USA, case reports and anecdotal evidence have also emerged from other countries, particularly the western European nations (5).

In 2023, the 'Monitoring the Future' survey funded by the National Institutes of Health in the USA included questions on delta-8-THC for the first time to assess its popularity among this vulnerable age group. The survey found that among the 2186 12th grade students included in the survey 11.4% reported previous year use of delta-8-THC products 35.4% of whom reported using delta-8-THC 10 or more times. Cannabis (marijuana) use was reported by 30.4% of students, while 91% of those who reported delta-8-THC use, also reported cannabis (marijuana) use (6).

With such indications of the rapidly rising popularity of delta-8-THC, concerns have been raised of the possibility of its evolution into a public health threat in the not-too-distant future. This calls for stronger monitoring of the available cannabis products and more effective regulation. While the use of delta-8-THC has not been reported in India, systems need to be set up to monitor the presence of this compound in cannabis used by Indian population.

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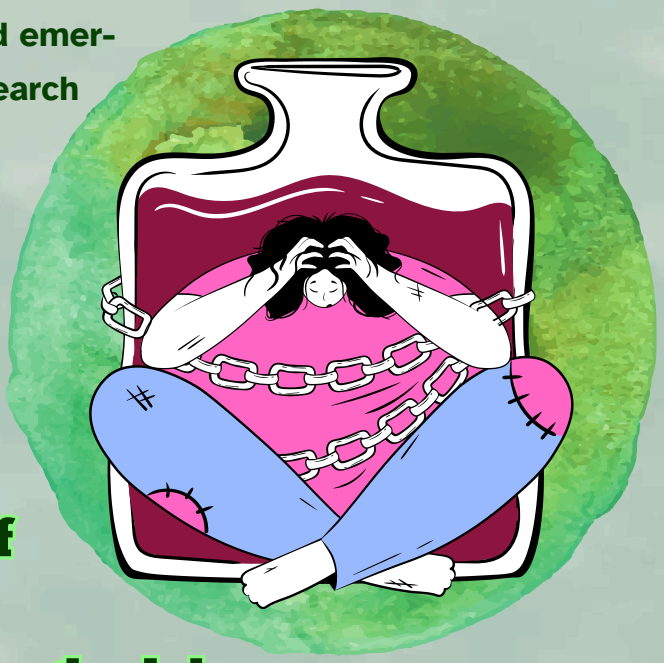
Special Populations

Piyali Mandal



Feminist research in addiction field is a new and emerging concept that is revolutionizing the way research is conducted for female participants. Feminist research is characterized by methodological innovations, reflexivity, and a focus on political change over adhering to procedural, epistemological, and disciplinary orthodoxy. The following article is an example of a feminist approach to conducting a research study in addiction.

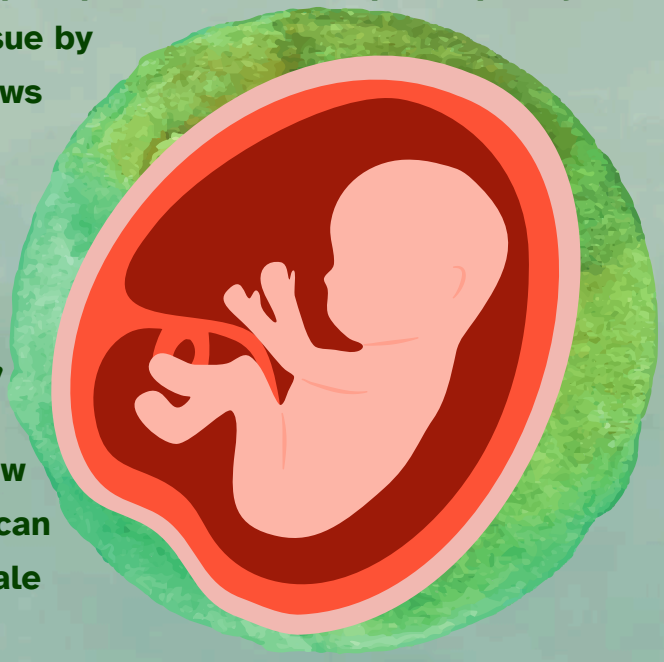
Understanding the experience of accessing treatment for women through feminist lens: A Novel methodology

An interesting research study, funded by the West Midlands Police Crime Commission in partnership with The JABBS Foundation and Staffordshire University in Britain, has been recently carried out at UK to understand women experiences of accessing community drug and alcohol treatment as well as associated professional experiences. Data collection was undertaken in three stages – In the first stage, individual and small-group interviews with professionals in the field (n = 17) were done by a female and a male researcher from a third-sector partner organisation (Centre for Justice Innovation). In the second stage, interviews and focus group discussions were conducted with two types of participants - (a) females who were in recovery and continuing to access community services for alcohol and drug use (n =28) and (b) practitioners who provide support for females accessing such services (n=5). Among these practitioners, 2 also had lived-in experience of taking services for their own alcohol or drug use in the past. In this phase, females conducted research interviews with the female participants. Also, the participants were offered the choice between an individual interview or a focus group discussion for discussing their sensitive health issues. This phase involved feminist approach along with participatory methodology. Feminist approach to research, according to the authors, include innovations in the research, reflexivity (critically reflecting upon their own biases and influences on

research outcome) and giving importance to political change rather than traditional procedural, epistemiological, and disciplinary norms.

Feminist approach stems from the current understanding that women experience 'oppression and exploitation' globally and usually experience drug and sex trafficking grooming predominantly by males. When females conduct research interviews with female participants, it reduces the power dynamics for the participants (giving importance to political change as well as reflexivity in research). In the current study, experts with lived experience not only co-produced research questions, but also co-facilitated data collection, which further helped in reducing the power dynamics (participatory approach). Also, the participants were offered the choice between an individual interview or a focus group discussion as the authors' felt that there would be a high possibility of traumatic experience disclosure (Innovations in research, and not strictly adhering to procedural / disciplinary norms).

In the third stage, world café method was used to collect data from professionals of drug and alcohol service and women's centres (n =9). World café is a participatory methodology, where participants explore an issue by discussing it in small groups. This method allows for cross-referencing data and co-designing of solutions.



The study found that stigma negatively impacted not only identification of treatment needs, but also the access to timely and appropriate service delivery. The study is an example of how feminist method of research in addiction field can be helpful to gather in-depth insights into female drug users (1).

Neonatal Opioid Withdrawal Syndrome (NOWS) and associated factors

Research on drug use during perinatal period has always been challenging due to ethical reasons. Hence there is scarcity of research data in this regard. A recent study from the USA adopted a retrospective design to analyse Neonatal Opioid Withdrawal Syndrome (NOWS) and its association with maternal and infant characteristics. In this case-control study, the diagnoses mentioned in the hospital medical records during discharge in Tennessee were used to identify NOWS cases (n = 1,369) in 2013 and 2014. Controls were randomly selected (n = 1,369) by matching the county of

residence and birth year. Maternal and infant characteristics were obtained by linking the data to birth certificate data. The study found that the mothers of infants with NOWS were more likely to be older, unmarried, and white than mothers of infants without NOWS. Additionally, these mothers faced higher health risks, including higher rates of smoking, hepatitis C virus (HCV) infection, herpes simplex diagnosis, and less frequent or no prenatal care. Infants with NOWS were more likely to have infections, be admitted to the NICU, have lower birth weights, be enrolled in state Medicaid program, and less likely to be breastfed compared to those without NOWS. The study also found that after adjusting for demographic factors and smoking, mothers of infants with NOWS had significantly higher odds of having HCV [OR=12.97 (95% CI 7.42, 22.66)]. This study highlights the importance of multifaceted prevention, and the need to conduct HCV testing among opioid dependent mothers and in NOWS infants (2).

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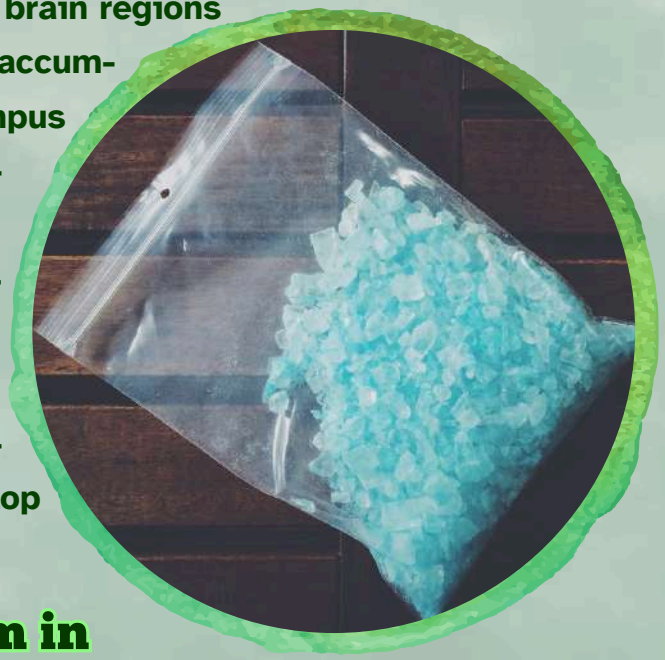
Newer Issues

Diptadhi Mukherjee, Vinit Patel



Neural circuit involved in reward include several brain regions including ventral tegmental area (VTA), nucleus accumbens (NA), prefrontal cortex (PFC), and hippocampus (HC). Orexin, a neuropeptide acts via two receptors (OX1R and OX2R). Orexin (hypocretin) neurons originate from lateral hypothalamus, extensively innervate VTA and NA and drive motivated behaviour, such as drug use. Recent studies have focussed on the orexinergic system's specific functions within these brain regions to develop new therapeutic targets for substance use.

Role of orexin/ hypocretin system in Methamphetamine use disorder

In a series of animal studies, researchers from Iran investigated the role of orexin receptor within the VTA (1,2) and cornu ammonis (CA-1) (3) in methamphetamine (METH) induced conditioned place preference (CPP).

First Study: Orexin-1 Receptor (OX1R) Antagonist in VTA

In the first study, 73 rats were randomly divided into two sets after the acquisition of METH induced CPP. The first set received various daily doses of OX1R antagonist, SB334867 dissolved in dimethyl sufoxide (DMSO) carrier (1, 3, 10 nmol/0.3µl DMSO per side) in bilateral VTA before each session throughout extinction phase. These rats showed significantly shorter extinction phase (mean extinction latency) at the highest dose (10 nmol; $p<0.001$), compared with controls and DMSO-only group, highlighting the role of OX1R receptor in extinction. The second set of rats received a single injection of antagonist (3, 10, 30 nmol/0.3µl DMSO per side) before the reinstatement phase. This led to prevention of METH induced reinstatement (10 nmol; $p<0.01$ and 30 nmol; $p<0.001$) compared to other groups, highlighting the role of OX1R receptor in reinstatement or relapse (1).

Second Study: Orexin-2 Receptor (OX2R) Antagonist in VTA

The same team then investigated the role of orexin 2 receptor (OX2R) in the reward processing. They randomly divided 109 rats into two groups. One group received daily injections of orexin 2 receptor (OX2R) antagonist, TCS OX2 29, during 10-day extinction phase (1, 3, 10 or 30nmol/0.3µl DMSO per side) or 12% DMSO. Significant reductions were observed in mean extinction latency period [$F(5,46)=12.80$; $p<0.0001$], with OX2R doses 10 and 30 nmol ($p<0.001$) compared to control. The second group received a single dose of OX2R antagonist before priming dose of METH on the reinstatement day. This single dose significantly reduced METH-induced CPP (3 nmol; $p<0.05$, 10 nmol; $p<0.01$, and 30 nmol; $p<0.001$) compared to controls, indicating that OX2R also has role in reinstatement or relapse (2).

Third Study: Orexinergic System in CA-1 Area

Moshrefi and colleagues investigated the role of the CA-1 area orexinergic system in acquisition and expression of METH induced CPP. Two groups of rats were administered different doses (1, 3, 10 or 30nmol/0.3µl DMSO per side) of selective OX1R and OX2R antagonists bilaterally into the CA-1 area. The dose administration was either daily during the conditioning phase or once during the post-conditioning phase and compared with DMSO only group or controls.

The results showed that both OX1R [10 nmol; $p<0.01$ and 30 nmol; $p<0.001$] and OX2R [10 nmol; $p<0.05$ and 30 nmol; $p<0.001$] antagonists during the conditioning phase blocked development of METH induced CPP in a dose-dependent manner. A single injection during the post-conditioning phase of OX1R antagonist [3 nmol; $p<0.05$, 10 nmol; $p<0.01$, and 30 nmol; $p<0.001$] and OX2R [30nmol; $p<0.01$] suppressed the expression of METH induced CPP (3).

These studies showed that antagonizing orexin receptors in the VTA and the CA-1 region of the hippocampus facilitated extinction, prevented reinstatement, and blocked the development and expression of METH-induced CPP.

Role of orexin / hypocretin in Opioid use disorder:

In another set of animal studies from America, researchers found that morphine increased the number, but reduced the size of orexin/hypocretin (Hrct+) neurons in the number, but reduced the size of orexin/hypocretin (Hrct+) neurons in the lateral hypothalamus. These effects lasted up to 4 weeks after withdrawing the morphine (4).

The researchers then investigated the effect of dual orexin receptor antagonist (DORA), suvorexant, on these opiate-induced changes. Suvorexant (administered at 30mg/kg in a 0.5% methylcellulose vehicle, 60 minutes before the morphine injections) blocked morphine's effect on both the number ($p=0.0001$) and size ($p=0.0001$) of Hrct+ neurons while preserving analgesia (at a dose of 30mg/kg), highlighting the less addictive option of pain management with a combination of opiates and DORAs (5).

These studies collectively provide a comprehensive understanding of the orexin system's intricate involvement in addiction-related behaviours. They underscore the potential of orexin modulation as a promising avenue for developing targeted pharmacotherapies for addiction treatment. However, generalization of findings from animal models to human addiction may not be straightforward due to differences in species and the complexity of human addiction. There is a need for further research to ensure safety, efficacy, and feasibility in humans.

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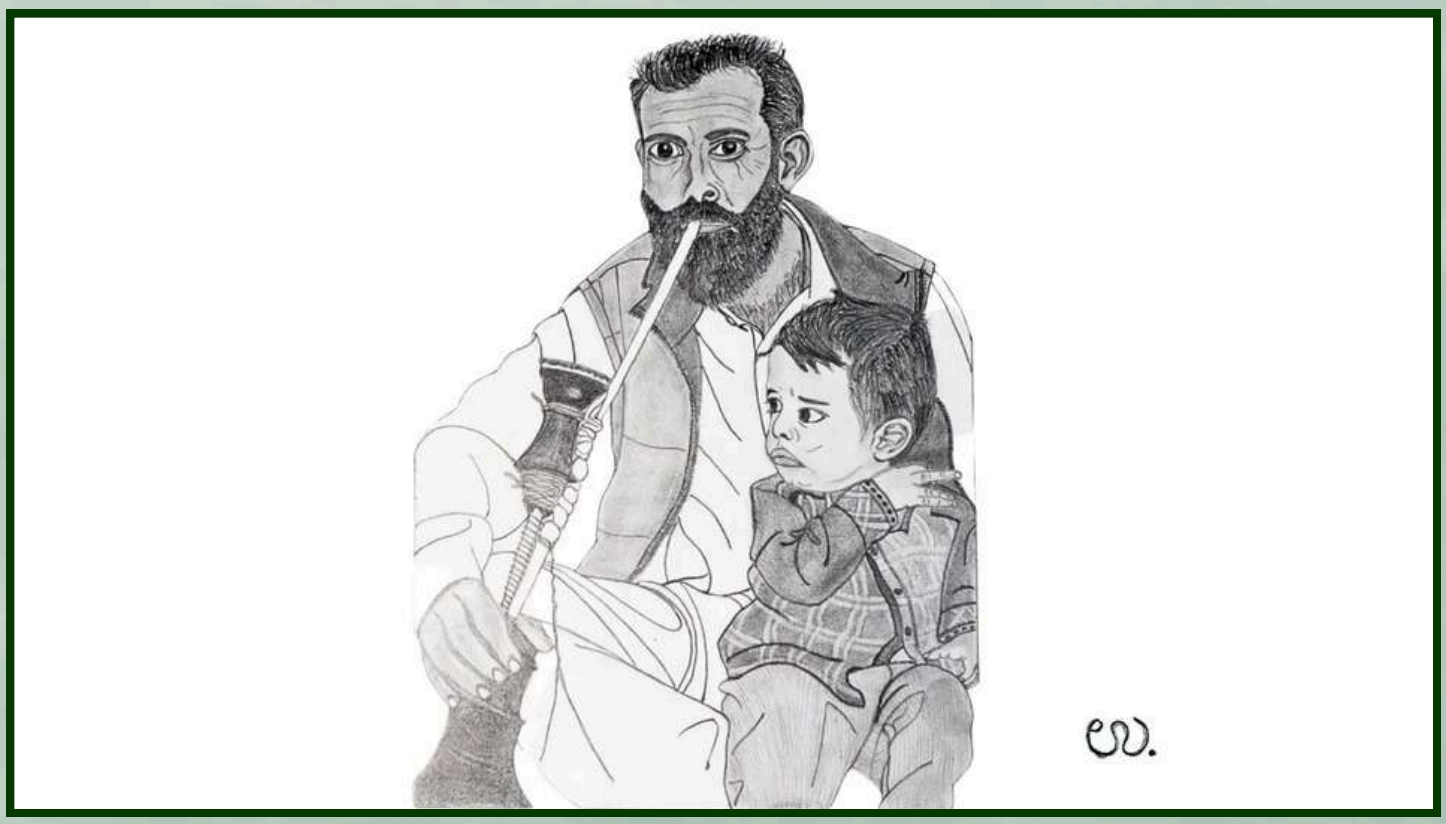
CREATIVE SECTION

Art Work
Hookah Smoking

Upendra Bhojani



This sketch is of a man and his son from a Gujjar Bakarwal tribe from Jammu & Kashmir. They live nomadic life moving high up the mountains in warmer seasons and retreating to plains in colder months looking for green pasture for their cattle. The man is smoking a Hookah (waterpipe), an apparatus used to heat tobacco (or cannabis, opium), the smoke of which is then passed through water before inhalation. Hookah was possibly invented in Mughal India by a Persian physician of Akbar (1542-1605 AD), who wanted to “purify” smoke when tobacco was first introduced to Akbar. Alternatively, it could have been invented in Persia even earlier and spread to India. At some point, sharing of a hookah became a way to socialize in groups. This habit that was prevalent among adults in rural India is now becoming popular among youth in cities. Smoking tobacco using Hookah is harmful for health, increasing the risk for cancers, heart diseases, lung diseases and many other illnesses. Sharing of hookah can also spread infectious diseases. Exposure to the smoke coming out of Hookah, often called passive smoking or second-hand smoking, as in the case of the child in this sketch, is also harmful for health. About one in ten adults (a total of 99.5 million) smoke tobacco in some form while about 0.7% of Indians smoke hookah. About one in ten youth are exposed to second-hand smoke at home while one in five youth are exposed to second-hand smoke at public places. This sketch is based on a photograph (CC license) by Syed QaaRif Andrabi.

Art Work
Digital Shackles

Vipindeep Kaur Sandhu

Art Work
Digital Shackles ... contd.

Vipindeep Kaur Sandhu

"Digital Shackles: Trapped in the Web, the Cost of Addiction to Social Media and Mobile Devices on Adolescent Minds"

Medium: Acrylic on canvas

Description:
The canvas piece "Digital shackles" explores the serious consequences of young people's addiction to social media and mobile devices, which might eventually result in mental health problems. The composition centers around a young child, his wrist bound by handcuffs intricately adorned with social media icons and symbols.The central motif of the artwork is a smartphone, its screen ablaze, child with head down and shoulders sagging. The child's stance, captures the profound sadness and vulnerability of a child, as if child is burdened by the weight of the world. The main focus of the piece is enormous handcuffs that are painstakingly made of metal, acting as a clear reminder of how much social media has impacted the child's life. The picture of a big hand is used to illustrate the crushing hold that social media addiction has on youth's life with chains sowing entrapment of child by social media
"Digital shackles" is a reminder of how critical it is to address the widespread effects of social media and smartphone addiction on children's mental health. The artwork challenges viewers to address the reality of our digital age and to fight for the welfare of future generations caught in the digital dystopia.

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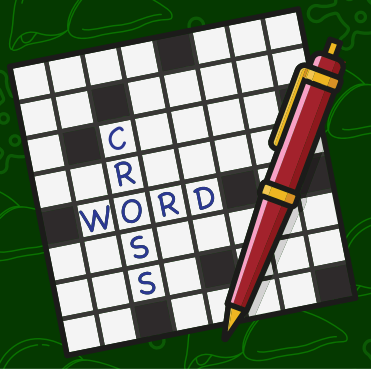
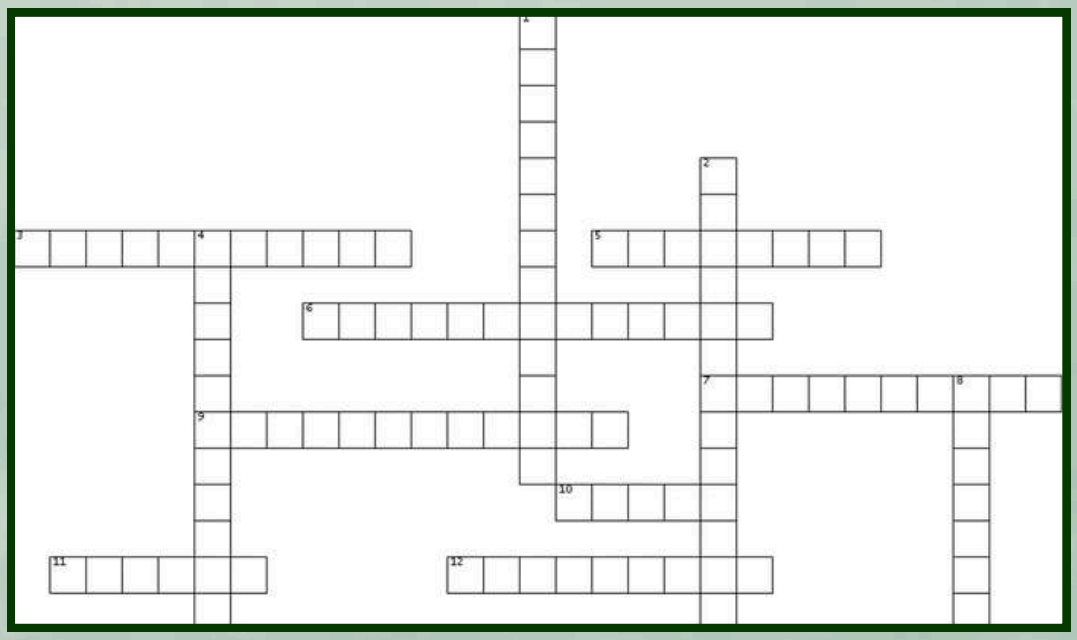
APSI Mindbender 3
Challenge Your Brain!!





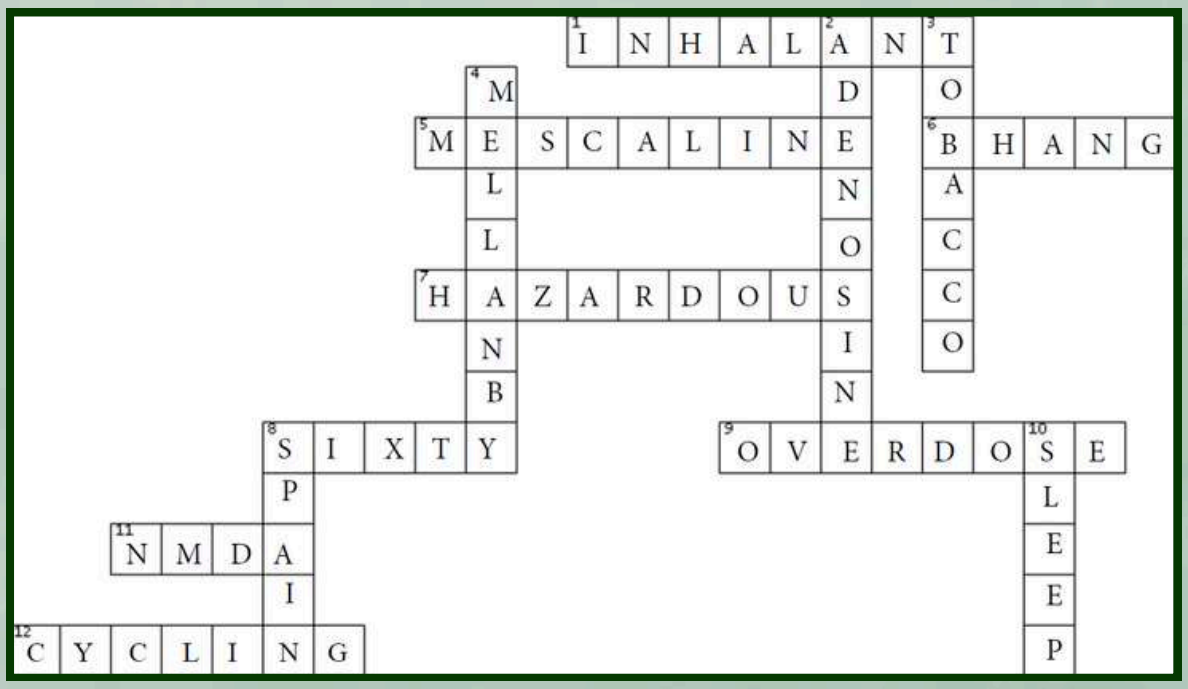
ACROSS

3. When a previously neutral stimuli after repeatedly pairing with drug withdrawal, it alone precipitates a withdrawal-like state, it is called as ____ withdrawal.
5. The enzyme inhibited by Disulfiram is ____ dehydrogenase.
6. The Stage of Change in which patient acknowledges the pros and cons of continued substance use but is ambivalent about change.
7. The first FDA approved game-based digital therapeutic device to improve attention among children with ADHD.
9. This term refers to a family member's harmful overinvolvement with the addiction process.
10. The Global ____ Programme was launched in 2008 by UNODC to monitor synthetic drugs problem and to design policies and programmes accordingly.
11. Most common form of smokeless tobacco used in India.
12. Benzodiazepines increase the ____ of GABA-Areceptor chloride channel opening.

DOWN

1. The opioid agonist maintenance medication found to be associated with shorter duration of Neonatal Abstinence syndrome in the MOTHER study.
2. A biological technique in which DREADDs are used to modulate neuronal activity.
4. Accelerated progression from initiation of substance use to development of substance use disorder.
8. When the effect of a substance increases over time with the same dose of substance, it is called as ____ tolerance.

Solution for APSI Mindbender 2



ACROSS

1. The only drug category where the prevalence among children and adolescents was found to be higher than adults in India
5. The major psychoactive substance in Peyote
6. The preparation of Cannabis that is not banned under NDPS act
7. A pattern of substance use that increases the risk of physical or mental harms according to ICD 11 is called as_____ substance use
8. Heavy episodic drinking refers to the use of ___ grams or more of pure alcohol on atleast one occasion in the past30 days
9. What does 'O' stand for in the SOS initiative by WHO-UNODC
11. The antagonist action at this receptor is responsible for reduced tolerance development in methadone
12. A pattern of drug use in which multiple doses of steroids are taken over a specific period of time, followed by stopping for a period, and starting again.

DOWN

2. Caffeine is an antagonist at _____ receptors
3. Deep TMS has been approved by FDA as an aid for short-term treatment for _____ smoking
4. Acute tolerance to alcohol is also called as _____ effect
8. Name of the country where the first cannabis social club was formed
10. Tobacco-induced _____ disorder is the only tobacco-induced disorder recognized in DSM 5

Upcoming Events

ADDICON 2024: Annual National Conference of APSI

Organised by: Sher-I-Kashmir Institute of Medical Sciences, Srinagar

When: 3 to 5 October 2024

Where: Srinagar, Jammu and Kashmir

Link: https://addicon2024.com/

International Society of Addiction Medicine 2024 Congress

Organised by: International Society of Addiction Medicine and Bağımlılık Psikiyatrisi Vakfı (Addiction Psychiatry Foundation of Türkiye)

When: 5 to 8 September 2024

Where: Istanbul, Turkey

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Share your Personal experience / Narrative / Painting / Poem

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Links to the Addiction Psychiatry Society of India below