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Drug addiction profile and monitoring liver functions tests of addicts at a specialized psychiatric treatment center

Abdelhak Ismail Benhaddou [1,2], Nazim Bellifa [1,2], Mohamed Yacine Achouri [1,2]

[1] Department of Pharmacy, Medical School Taleb Mourad, University of Sidi Bel Abbes 22000, Algeria
[2] University Hospital Center Dr Hassani Abdelkader, Toxicology Laboratory, Sidi Bel Abbes 2200, Algeria

ORCID ID of the author(s)
AIB: 0000-0002-6322-5907
NB: 0000-0002-4247-1850
MYA: 0000-0003-3765-8642

Corresponding Author
Abdelhak Ismail Benhaddou
Colonel Othmane Avenue. Sidi Bel Abbes 22000. Alegria
E-mail: benhaddou13ismail@gmail.com
ismail.benhaddou@univ-sba.dz

Ethics Committee Approval
The Scientific and Ethical Committee of the Department of Pharmacy, Faculty of Medicine. Reference number: 05/DPH/FC/SEC/2020. Date: 21/March/2020. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Drug addiction a public health problem, which Algeria cannot escape from. According to the Algerian National Office for the Fight Against Drug Abuse and Addiction (ONLCDT), 9,680 drug addicts were treated in the first half of 2019. The lack of information and prevalence data continues to impede determining the extent of drug use in Africa. This study aims to determine the profile of drug abuse consumption in a specialized psychiatric treatment center and identify the impact of drug use on the disruption of liver function in patients admitted to the center in 2019.
Methods: In this retrospective cohort study, we used the data of 80 drug addicts in statistical analyses.
Results: Males were more prevalent than females (92% vs 8%), and most patients were living in urban areas (67%). The majority were married (84%) and unemployed (58%). The ages of most addicts (52%) ranged between 21 - 40 years. The mean duration of drug use was 5.15 years (SD=2.3). Cannabis was the most prevalent (n=34, 20%) drug used, followed by ecstasy (MDMA) (n=28, 17%), and others (cocaine 15%, alcohol 15%, amphetamine 10%, benzodiazepine 11%, LSD 10%, nicotine 6%). The mean number of drugs abused per patient was 2.35. The most marked observation from data comparison was the significant correlation between drug abuse duration and liver function tests (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, bilirubin) ($P<0.05$). Hepatic serology results show that 16% and 7.5% were hepatitis C and hepatitis B positive, respectively.
Conclusion: Given the differences in sociodemographic and drug addiction, further studies involving a large population are needed to identify the factors associated with drug addiction. Algeria has few rehabilitation centers, all of which are limited in clinical capacities and need to be improved.

Keywords: Drug addiction, Liver functions tests, Epidemiology, Drug treatment center

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Introduction

Drug addiction has become a serious public health issue. According to the most recent global drug survey in 2019, 35 million people worldwide suffer from drug-related disorders, while only 1 in 7 people worldwide receive treatment. Eleven million people injected drugs in 2017, 1.4 million of which were HIV and 5.6 million of which were hepatitis C positive, as reported by the United Nations Office on Drugs and Crime (UNODC) [1]. According to the Algerian National Office for the Fight Against Drug abuse and Addiction (ONLCDT), 9,680 drug users were treated in the first half of 2019. Algerian drug policy is aimed at minimizing drug supply and sale, although promising standards are set for regulation, prevention, and treatment [2]. The lack of information and prevalence data also impedes the assessment of drug use in Africa.

Drug consumption usually causes liver injury, and in some cases, there are almost no signs, which may result in further damage and lack of early diagnosis. All addictive drugs such as alcohol may have adverse effects [3]. Liver injury caused by drugs is diagnosed with elevated levels of hepatic enzymes and bilirubin [4]. Our research aimed to evaluate the drug abuse profile in a specialized psychiatric treatment center and identify the impact of drug use on the disruption of liver function in patients admitted to the center in 2019. Estimating the prevalence of regional drug use is critical in measuring the amount and severity of this health problem. Decisions regarding the provision of medical services by governments, decision-makers, and funding should be made based on these data [5].

Materials and methods

The population of this retrospective cohort study is composed of 80 drug abuse patients who presented to the treatment and detoxification center of Oran, located in North West Algeria, from January 2019 to January 2020.

Addiction assessment criteria were based on DSM-5 (Diagnostic and Statistical Manual of Mental Disorders). The patients self-reported the drugs consumed, and the following liver function tests were obtained to establish the relationship between drug use and liver function disorders: Bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT) and hepatic serology. Any patient admitted to the psychiatric treatment center regardless of sociodemographic characteristics and drug use were included in the study, and those with any other liver diseases were excluded. Upon admission, a toxicology and medical report was drawn up for each patient, containing the socio-demographic information, type of drug addiction, liver function tests, and withdrawal treatment.

Statistical analysis

Statistical analysis was performed by Excel 2013 and SPSS V25, and significance was analyzed with linear correlation coefficient r and P-value. The bibliographic references were managed by the Mendeley software.

Results

Sociodemographic characteristics

We used the data of 80 patients in statistical analyses. Males were more prevalent than females (92% vs 8%), and most patients were living in urban areas (67%). The majority were married (84%) and unemployed (58%). The mean duration of drug use was 5.15 years (SD=2.3), with 45% of patients with a history of drug abuse for more than 5 years (Table 1).

Table 1: Repartition of Socio-demographic characteristics of drug addicts

Socio-demographic characteristics		n= 80	% (prevalence)
Gender	Male	74	92
	Female	06	08
Marital situation	Single	67	84
	Married	13	16
Education level	Primary	09	11
	Middle	36	45
	Secondary and more	35	44
Profession	Unemployed	46	58
	Employed	34	42
Duration of drug use	< 2 year	17	21
	2 - 5 year	27	34
	> 5 year	36	45
Age range	< 20 year	17	21
	20 - 40 year	41	51
	41 - 60 year	18	23
	> 60 year	04	05
Habitat	Urban	54	67
	Rural	26	33

Prevalence of drugs-use

Cannabis was the most prevalent (n=34, 20%) drug used, followed by ecstasy (MDMA) (n=28, 17%), alcohol and cocaine (15% for both), benzodiazepine (11%), and amphetamine (n=16, 10%). LSD and nicotine use were less prevalent (10% and 6%, respectively) (Figure 1).

Polydrug addiction

The mean number of drugs used among patients was 2.35, the rate of any polydrug (2 or 3 drugs) use was 92% (n=74) (Figure 2).

All patients were dependent both physically and psychologically (n=80, 100%).

Drug treatment

The main therapy protocol used in our study consists of fluoxetine (n=54, 34%), amitriptyline (n=52, 32%) and carbamazepine (n=42, 26%), and levomepromazine secondarily (n=13, 9%) (Figure 3).

Figure 1: Distribution of frequency of drug used

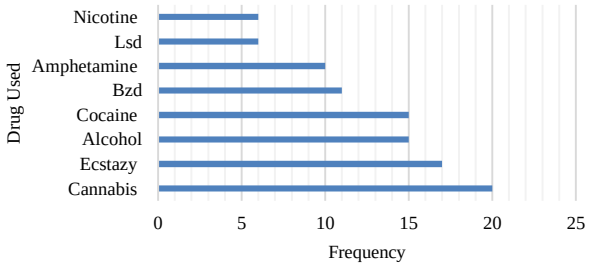


Figure 2: Distribution of prevalence of polydrug addiction

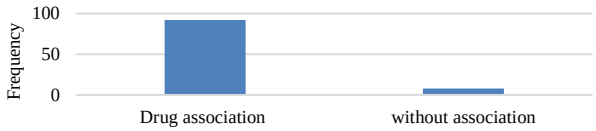
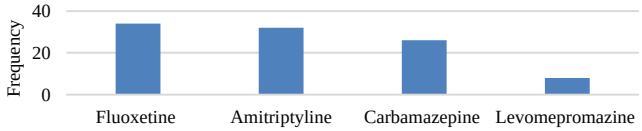


Figure 3: Distribution of the prevalence of drug treatment



Liver function tests

Results of liver function tests are represented as boxplot. The mean values of aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, alkaline phosphatase (ALP), and gamma-glutamyl transferase (GGT) were 73.75 UI/L (Med=65, Min=31, Max=166), 68 UI (Med=61.5, Min=27, Max=159), 43 UI (Med=40.5, Min=19, Max=93), 210 UI (Med=202, Min=139, Max=328), and 72 UI (Med=69.5, Min=45, Max=105), respectively (Figures 4-8).

Figure 4: Measures of position AST

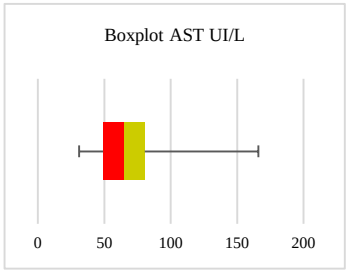


Figure 5: Measures of position ALT

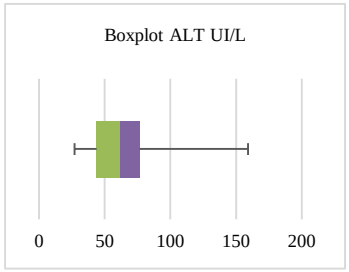


Figure 6: Measures of position Bilirubin

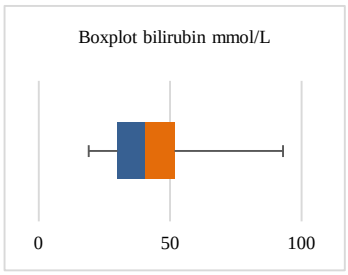


Figure 7: Measures of position ALP

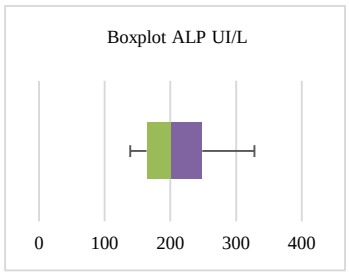
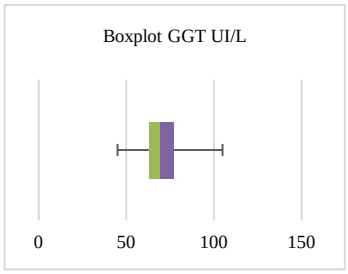


Figure 8: Measures of position GGT



The relationship between the duration of drug use and various biological parameters (AST, ALT, ALP, GGT, and Bilirubin) of the liver were determined with a linear correlation curve, calculating the p-value (p) and the linear correlation coefficient (r) for each variable (Figure 9). There were significant correlations between changes in AST (r = 0.76, $P<0.05$), ALT (r = 0.78, $P<0.05$), Bilirubin (r = 0.85, $P<0.05$), GGT (r =0. 86, $P<0.05$), ALP (r=0.53, $P<0.05$) and drug abuse.

Hepatitis serology

Among all, 16% were hepatitis C and 7.5% were hepatitis B positive, while all patients were hepatitis A negative (Figure 10).

Figure 9: Correlation between liver function tests and duration of drug use

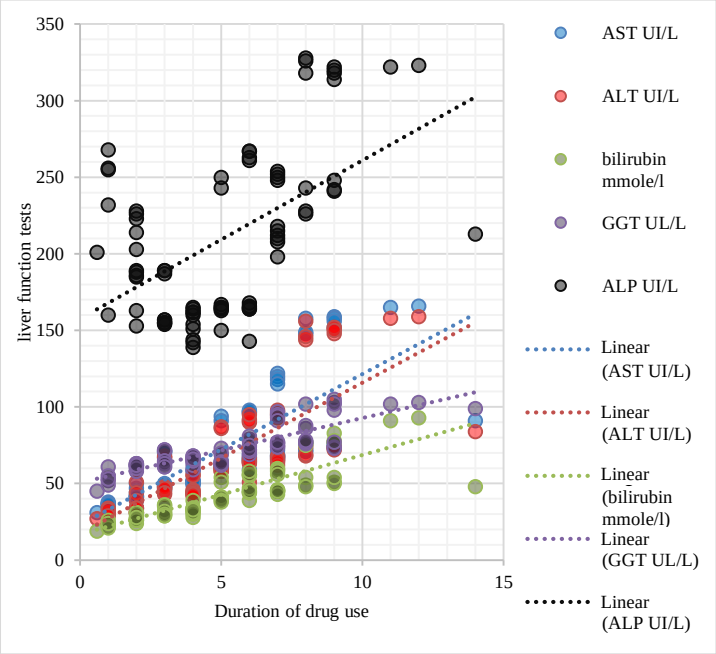
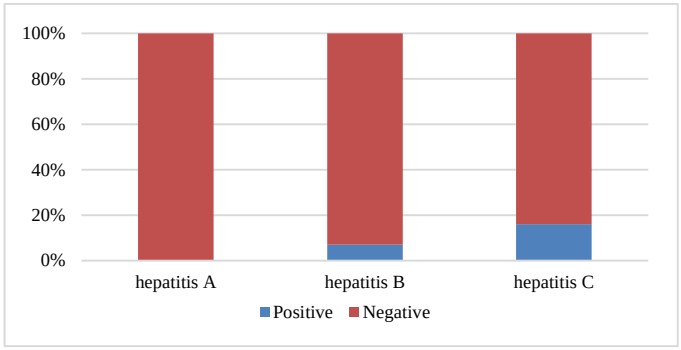


Figure 10: Repartition of frequency of hepatitis serology



Discussion

Socio-demographic characteristics of drug addicts

The mean age of patients admitted to the psychiatric center was 32.5 years, 92% were male and most patients' age ranged between 21 – 40 years (51%). Gender disparities were significant ($P<0.05$). Multiple studies have consistently shown that substance abuse is a youth problem [6,7]. Similar to ours, a Turkish study revealed a higher proportion of males (82.4%, n=1623) than females (17.6%, n=346) [8].

According to a survey, the mean age of drug addicts admitted to a private clinic in the Accra Metropolis (GHANA) was 29.24 years, 80% were males, and 33.3% had left school at the secondary level [9].

We can confirm that drug addiction is a male problem, and gender differences have always been present. The inequality in gender distribution may be due to, some degree, the innate differences between sexes in their readiness to learn certain behaviors. Males are associated with aggression, violence, independency, and adventurism, which are potent factors in the initiation of drug addiction [10].

Forty-five percent of patients have a drug consumption history exceeding 5 years. Puberty is commonly considered a critically risky period for the initiation of drug-use, with multiple studies showing associations between age at first drug-use and the occurrence of abuse or dependence. Drug addiction is increased among individuals who began the use of such

substances in puberty or early adolescence than most of those beginning use during adulthood [11, 12].

Single patient frequency is highest (84 %) compared to married patients. Several studies have shown that marriage accelerates a decrease in drug use when compared to those who remain single. N. Sinha concluded that marriage was cited as a protective factor against drug use, but this has been affected by several factors, such as quality spare time, a more mature relationship, a sense of responsibility, and intimacy [13].

The education levels of 66% of patients in our study is quite low. The causes often include ignorance, which may account for this elevated level of dropouts at secondary school due to drug abuse. Galea et al. [14] concluded that there is a connection between the level of addiction and level of education.

In our study, most drug abusers are unemployed. Work decreases drug abuse, and entry into the workplace seems to be an opportunity to abandon drug use for most people [15].

Majority of our patients live in urban areas (67%), which could be a factor promoting drug use. According to Galea et al. [16], urban residents are more numerous than those in rural areas. Immigration to cities, linked to industrialization and modernization, has been described as a contributing factor to drug addiction, creating favorable conditions for both widows and drug users.

Several studies have shown the relationship between increased drug use and different socio-demographic characteristics (gender, age, habitat, marital status, poverty, low education level, onset of use) [17-19]. Our results are almost similar to the results of a Moroccan study focused on the epidemiological specificities of psychiatric patients [20].

Drug use profile

Cannabis is the most common drug used in our study (20%). Algeria is a transit country for cannabis, and in 2018, 31,936,386 kg of cannabis resin was seized according to the Algerian National Office for the Fight Against Drug abuse and Addiction [21].

During 2018, according to the INCB report, at least 16 countries from all regions of Africa reported seizures of cannabis herb, resins, and plants. Cannabis continues to be the main drug of abuse [22].

In the European Union, cannabis is the most widely tried substance (55.4 million males and 36.1 million females), lifetime cannabis use levels vary considerably from one country to another, ranging from about 4% of adults in Malta to 45% in France [23]. In 2007, the European school survey on alcohol and other drugs (ESPAD) indicated that 31% of 16-year-olds recognized that they had already smoked cannabis in their lifetime, this influence of early entry into drug use can be linked to social problems, school failure, or delinquency [24]. A similar research in Turkey clarified that cannabis was the most prevalent drug used (60.1%) followed by solvents/inhalants (38.3%) and ecstasy (33.4%) [8]. Cannabis is still the most used drug in Côte d'Ivoire, and it affects more than 93.75% of the population using illicit drugs [25].

The second most consumed drug in our study is Ecstasy/MDMA (3, 4-methylenedioxy-N-methylamphetamine) (17%). The use of "ecstasy" over the past year is estimated at 21.3 million people globally, corresponding to 0.4 percent of the global population aged 15–64. Past year use of "ecstasy" is relatively high in Oceania (2.2 percent for Australia and New Zealand), West and Central Europe (0.9 percent), and North America (0.9 percent) [26]. According to a study by Li-Tzy W concerning the potential heterogeneity of ecstasy or MDMA users, approximately 1.6% (n=562) of adult participants (N=43,093) reported lifetime ecstasy use [27].

Cocaine consumption in our study took third place, along with alcohol, at 15%. Globally, an estimated 18.1 million people were past-year users of cocaine in 2017, corresponding to 0.4 percent of the global population aged 15–64. Past-year use of cocaine is high in Oceania (2.2 percent for Australia and New Zealand), North America (2.1 percent), Western and Central Europe (1.3 percent), and South America (1.0 percent). In parts of Asia and West Africa, increasing amounts of cocaine have reportedly been seized, which indicates that cocaine use could potentially increase, especially among the affluent, urban segments of the population, in sub-regions where such use had previously been low [26]. The annual global average alcohol consumption in 2016 is 6.4 liters per person older than 15, in Algeria, it represents a low level of 0.9 liters per person [28].

We see wide geographical differences. Alcohol consumption is particularly low in many countries across North Africa and the Middle East, close to zero. At the upper end of the scale, alcohol consumption across Europe is highest at around 15 liters per person per year [29].

Globally, alcohol dependence was the most prevalent drug of dependence, with 63.5 million (57.5- 69.9) estimated cases in 2015, and an age-standardized average of 843.2 (763.7-927.3) per 100 000 people [30].

The prevalence of alcohol use in the United States is estimated to be approximately 48% for those aged 12 years and older, with almost 8% of those aged 12 to 20 engaging in binge drinking (National Institute on Alcohol Abuse and Alcoholism) [NIAAA] in 2017.

Although benzodiazepines are invaluable in the treatment of anxiety disorders, they have some potential for abuse and may cause dependence or addiction, as indicated by our study estimation at 11%. Intentional abusers of benzodiazepines usually have other drug abuse problems. Benzodiazepines are typically a secondary drug addiction used mainly to increase the high concentration from another drug or to offset the adverse effects of other drugs. The legitimate use of benzodiazepines leads to few cases of addiction [31].

As per Lagnaoui, R. the prevalence of current use of BZD was 7.5%. It was higher among women (9.7%) than men (5.2%), and among the unemployed, and increased with age. The duration of BZD use was more than 6 months in 75.9% of users [32].

Problems related to intravenous amphetamine use have historically been more acute in the countries of Northern Europe. By contrast, methamphetamine problems are more evident in the Czech Republic and Slovakia. According to a 2015 estimate for Germany, 0.19% of adults use amphetamines. Amphetamine users are likely to make up the majority of the 2,234 consumers with stimulant issues (0.18%) reported in Latvia in 2017. In the Czech Republic, the problematic use of methamphetamine in adults (aged 15 to 64) was estimated at 0.50% in 2017 (34,700

users). Estimate for Cyprus was 0.03%, or 176 consumers. Amphetamines are the drugs for which the gender gap is lowest [23].

While regular use of hallucinogenic and dissociative drugs, in general, has remained relatively low in recent years, one study reported that the United States ranks first among 36 nations in the proportion of high school students ever using LSD or other hallucinogens in their lifetime (6 percent versus 2 percent in Europe) (Hibell, 2012) [33].

Tobacco smoke has been included in our study for nicotine addiction, which represents 6% of other drugs. A retrospective, descriptive, and comparative study of all patients treated in the smoking unit of the University Hospital Complex of Albacete during the years 2008-2012 included 1484 patients, of which 48.6% were female. The mean age was 46.8 years, and the mean age of starting smoking was 17.6 years. The mean number of previous attempts to quit was 1.48, and the mean number of cigarettes smoked was 25.39 [34]. The proportion of tobacco consumption in the Ivory Coast lie between 27.5% and 36% in the general population and between 14% and 24% among high school students [25].

Polydrug addiction

The 2018 National Survey on Drug Use and Health, produced by the Nigerian government with support from the European Union and UNODC and released in January 2019, is the first-ever comprehensive survey of drug use conducted in the country. It analyses data collected from 38,850 households and 9,344 high-risk drug users. The report found that in drug addiction, polydrug use was very common, as nearly 95 percent of high-risk users and almost half of other users reported having consumed more than one drug in the previous year [22], like our study, in which 92% of patients are polydrug users. The proportion of any polysubstance use was 60.2% (n=1185) in another study conducted in the child and adolescent dependence center in Istanbul, Turkey [8]. Contrary to these findings, studies from developed countries reported a lower rate of polysubstance use in treatment-seeking children and adolescents. The rate of polysubstance use was 45% in a study conducted in a dependence center in Australia [35].

Treatment

Determining the prevalence of drug addiction and dependence is the means to initiate appropriate treatment and intervention coverage [36]. Addiction is a chronic disease that tends to recur when treatment is interrupted, thus, long-term treatment is recommended. The same principles apply in the detoxification from nicotine dependence using nicotine replacement and from sedative (ethanol) dependence using another sedative such as a benzodiazepine. Withdrawal of the stimulant (cocaine and amphetamine) typically requires no treatment, but rapid return to drug use is frequent [37].

The treatment of addicted patients must always be individualized. This requires a complete evaluation so that coexisting medical, psychiatric, and social problems can be addressed as needed. The types of medications that have demonstrated efficacy in combination with behavioral therapy in the prevention of relapse can be classified as agonists (including partial agonists), antagonists, and anti-craving medications that work through a variety of mechanisms. Vaccines are an experimental approach that is currently being evaluated in clinical trials [38, 39].

The therapy used in our study is levomepromazine (8%) for the treatment of psychotic disorders, fluoxetine (34%) and amitriptyline (32%) for depressive disorders and carbamazepine (26%) for bipolar disorders.

Liver function tests

Patients with substance use disorders are at increased risk of a range of medical and psychiatric disorders. Levels of consumption can still contribute to end-organ (i.e., liver) damage [40].

Liver function tests (LFTs) refer to measurements of serum bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transpeptidase (GGT) [41]. Increased serum liver enzymes, alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyl transferase (GGT) are markers of inflammation and oxidative stress, for detecting alcohol and drug use [42]. Among the drugs that can also cause liver disorders are cocaine and MDMA [43].

Ninety-eight percent of patients in our study have increased AST, 96% have increased ALT, 100% have increased GGT, 99% have positive ALP and 99% have increased bilirubin levels. The correlation between these results and the duration of drug abuse use is significant for all liver function tests, demonstrating the increase of these enzymes with the increase of the duration of consumption ($P<0.05$).

A recent global systematic review including 55671 records in 179 countries reports that globally, an estimated 15.6 million people injected drugs in 2015, 8.2 million of which were HCV antibody, and 1.4 million people of which were HBsAg positive. This is equivalent to 52.3% and 8.9% of people who inject drugs globally, respectively. In East and North Africa, 48.1% of individuals who inject drugs are HCV and 8.1% are HBV positive [44]. Our study also showed that HCV prevalence (16.2%) is higher than that of HBV (7.5%).

The UNODC World Drug Report stated that among drug-injectors, 51.7%, equating to 6.1 million people, were HCV-positive, and 13.1%, equating to 1.6 million, were HBV-positive [45].

Conclusions and recommendations

The increase in drug addiction in Algeria seems to be concomitant with its progress on a global level and is linked to the economic, social, and cultural crises the country faces. This is not a reason to stay away from the study's issues. We can help to solve these anomalies; several recommendations are proposed:

- Organize awareness sessions in the school and university environment. Knowing that most of the consumption begins in adolescence, prevention targeting this population is a priority.
- Generate appropriate support and publication on the impact of drug use on the liver and ensure dissemination to the broadest spectrum inside the society.

The present study overcomes a major limitation of the national surveys. Given the differences in sociodemographic and drug addiction, further investigation is necessary to identify the factors associated with drug addiction. There are few drug use

treatment centers in Algeria, which are constrained in clinical and therapeutic capacities. The service will have to be extended.

References

1. AUnited Nations on Drug and Crime (UNODC). World Drug Report 2019 [Internet]. [cited 2020 Apr 18]. Available from: https://wdr.unodc.org/wdr2019/
2. Algerian National Office for the Fight against Drug abuse and Addiction (ONLCDT); Satististical review of the first eleven months of 2019 [Internet]. [cited 2020 Apr 22]. Available from: https://onlcdt.mjustice.dz/onlcdt_fr/donnees_statistiques/bilan[2019].pdf
3. Donepudi I, Massoumi H, Dharmarajan TS, Pitchumoni CS. Drug-induced liver injury. Geriatr Gastroenterol. 2012;409–20. doi: 10.1007/978-1-4419-1623-5_41
4. Björnsson E, Kalaitzakis E, Olsson R. The impact of eosinophilia and hepatic necrosis on prognosis in patients with drug-induced liver injury. Aliment Pharmacol Ther. 2007;25(12):1411–21. doi: 10.1111/j.1365-2036.2007.03330.x
5. Degenhardt L, Hall W. Extent of illicit drug use and dependence, and their contribution to the global burden of disease. Lancet. 2012;379(9810):55–70. doi: 10.1016/S0140-6736(11)61138-0
6. Kamali EP. Felony and the Guilty Mind in Medieval England. Cambridge University Press 2019;348:1–30. https://doi.org/10.1017/9781108670890
7. Byrd RS, Weitzman M, Doniger AS. Increased drug use among old-for-grade adolescents. Archives of Pediatrics & Adolescent Medicine. 1996;150(5):470-6. doi: 10.1001/archpedi.1996.02170300024006
8. Demirci AÇ, Erdoıan A, Yalçin Ö, Yildizhan E, Koyuncu Z, Eseroılu T, et al. Sociodemographic characteristics and drug abuse patterns of adolescents admitted for substance use disorder treatment in Istanbul. Am J Drug Alcohol Abuse. 2015;41(3):212–9. doi: 10.3109/00952990.2014.973961
9. Lamptey.JJ. Sociodemographic caractéristique of substances abusers admitted to a private specialist clinic. Ghana Medical Journal. 2005;39(1). doi: 10.4314/gmj.v39i1.35973
10. Gradus JL, Leatherman S, Curreri A, Myers LG, Ferguson R, Miller M. Gender differences in substance abuse, PTSD and intentional self-harm among veterans health administration patients. Drug Alcohol Depend. 2017;171:66–9. doi: 10.1016/j.drugalcdep.2016.11.012
11. Lopez-Quintero C, Cobos JP de los, Hasin DS, Okuda M, Wang S, Grant BF, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: Results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Drug Alcohol Depend. 2011;115(1–2):120–30. doi: 10.1016/j.drugalcdep.2010.11.004
12. Chen CY, Storr CL, Anthony JC. Early-onset drug use and risk for drug dependence problems. Addict Behav. 2009;34(3):319–22. doi: 10.1016/j.addbeh.2008.10.021
13. Namita S. Effect of marital status on substance abuse. International Journal of Recent Scientific Research. 2018. 9(5), pp. 27012-27015. doi: 10.24327/ijrsr.2018.0905.2168
14. Galea S, Ahern J, Tracy M, Rudenstine S, Vlahov D. Education inequality and use of cigarettes, alcohol, and marijuana. Drug Alcohol Depend. 2007;90(SUPPL. 1):4–15. doi: 10.1016/j.drugalcdep.2006.11.008
15. Henkel D. Unemployment and substance use: A review of the Literature (1990-2010). Curr Drug Abuse Rev. 2011;4(1):4–27. doi: 10.2174/1874473711104010004
16. Galea S, Rudenstine S, Vlahov D. Drug use, misuse, and the urban environment. Drug Alcohol Rev. 2005;24(2):127–36. doi: 10.1080/09595230500102509
17. Zhou Y, Zhao M, Zhou C, Li R. Sex differences in drug addiction and response to exercise intervention: From human to animal studies. Front Neuroendocrinol. 2016;40:24–41. doi: 10.1016/j.yfrne.2015.07.001
18. Vederhus JK, Kristensen Ø, Timko C. How do psychological characteristics of family members affected by substance use influence quality of life? Qual Life Res. 2019;28(8):2161–70. doi: 10.1007/s11136-019-02169-x
19. Argyriou E, Um M, Carron C, Cyders MA. Age and impulsive behavior in drug addiction: A review of past research and future directions. Pharmacol Biochem Behav. 2018;164:106–17. doi: 10.1016/j.pbb.2017.07.013
20. Belghazi D, Moussaoui D, Kadri N. Spécificités épidémiologiques, cliniques et culturelles des patients hospitalisés au centre psychiatrique universitaire Ibn-Rochd de Casablanca. Ann Med Psychol (Paris). 2016;174(2):100–4. doi: 10.1016/j.amp.2013.07.008
21. Algerian National Office for the Fight against Drug abuse and Addiction (ONLCDT); statistical review of 2018 [Internet]. [cited 2020 Apr 29]. Available from: https://onlcdt.mjustice.dz/onlcdt_fr/donnees_statistiques/bilan[2018].pdf
22. International Narctics Control Board ; Report of the INCB for Africa of 2019;66–70 [Internet]. [cited 2020 Apr 29]. Available from: https://www.incb.org/documents/Publications/AnnualReports/AR2019/Annual_Report_Chapters/AR2019_Chapter_III_Africa.pdf
23. European Monitoring Center for Drugs and Drug addicition; European drug report Lisbon, June 2019. ISBN 978-92-9497-398-6. doi: 10.2810/191370
24. Legleye S, Spilka S, Le Nezet O, Hassler C, Choquet M. Alcool, tabac et cannabis à 16 ans - Evolutions, usages récents, accessibilité et modes de vie. Premiers résultats du volet français de l'enquête ESPAD 2007. Tendances. 2009;(64):1–6.
25. Soumahoro MK, Kouassi PD, Ipou SY, Mian NNA, Ouattara A, Dosso M. Épidémiologie De La Consommation Des Substances Psychoactives En Côte D ' Ivoire : Revue Systématique De La Littérature Epidemiology of Psychoactive Substances Consumption in Ivory Coast : systemic review study. 2018;34–42.
26. United Nations Office on Drugs and Crime (UNODC). Global overview of drug demand and supply. United Nations, June 2019. ISBN: 978-92-1-148314-7. Available from: https://wdr.unodc.org/wdr2019/prelaunch/WDR19_Booklet_2_DRUG_DEMAND.pdf
27. Wu LT, Parrott AC, Ringwalt CL, Yang C, Blazer DG. The variety of ecstasy/MDMA users: Results from the national epidemiologic survey on alcohol and related conditions. Am J Addict. 2009;18(6):452–61. doi: 10.3109/10550490903206049
28. WHO. Global information system on alcohol and health (GISAH). 2016. [cited 2020 May 1]. Available from: https://www.who.int/substance_abuse/activities/gisah/en/
29. WHO. Global Health Observatory data repository [Internet]. [cited 2020 May 2]. Available from: https://apps.who.int/gho/data/?theme=main
30. Peacock A, Leung J, Larney S, Colledge S, Hickman M, Rehm J, et al. Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. Addiction. 2018;113(10):1905–26. doi: 10.1111/add.14234
31. Salzman C. Addiction to benzodiazepines. Psychiatr Q. 1998;69(4):251–61.
32. Lagnaoui R, Depont F, Fourrier A, Abouelfath A, Bégaud B, Verdoux H, et al. Patterns and correlates of benzodiazepine use in the French general population. Eur J Clin Pharmacol. 2004;60(7):523–9. doi: 10.1007/s00228-004-0808-2
33. Hibell B, Guttormsson U, Ahlström S, Balakireva O, Bjarnason T, Kokkevi A, et al. The 2011 ESPAD Report: Substance Use Among Students in 36 European Countries. 2012. 394 p. ISBN: 978-91-7278-233-4
34. Godoy R, Callejas FJ, Cruz J, Tornero AI, Tárraga PJ, Rodríguez-Montes JA. Comparative analysis: Effectiveness of nicotine addiction treatment in people with psychiatric comorbidity. Semergen. 2018;44(4):249–56. doi: 10.1016/j.semerg.2017.03.008
35. Phillips NL, Milne B, Silsbury C, Zappia P, Zehetner A, Klineberg E, et al. Addressing adolescent substance use in a pediatric health-care setting. J Paediatr Child Health. 2014;50(9):726–31. doi: 10.1111/jpc.12622
36. Gowing LR, Ali RL, Allsop S, Marsden J, Turf EE, West R, et al. Global statistics on addictive behaviors: 2014 status report. Addiction. 2015;110(6):904–19. doi: 10.1111/add.12899
37. O'Brien CP. Evidence-based treatments of addiction. Philos Trans R Soc B Biol Sci. 2008;363(1507):3277–86. doi: 10.1098/rstb.2008.0105
38. Sofuoglu M, Kosten TR. Emerging pharmacological strategies in the fight against cocaine addiction. Expert Opin Emerg Drugs. 2006;11(1):91–8. doi: 10.1517/14728214.11.1.91
39. Martell BA, Mitchell E, Poling J, Gonsai K, Kosten TR. Vaccine pharmacotherapy for the treatment of cocaine dependence. Biol Psychiatry. 2005;58(2):158–64. doi: 10.1016/j.biopsych.2005.04.032
40. WHO. Pharmacological treatment of mental disorders in primary health care. World Health Organization 2009. ISBN 978 92 4 154769 7 https://apps.who.int/iris/handle/10665/44095
41. Hurley J, Green JT. The Liver. SEVENTH ED. Brocklehurst's Textbook of Geriatric Medicine and Gerontology. Elsevier; 2010. 635–644 p. doi: 10.1016/B978-1-4160-6231-8.10078-9
42. Leggio L, Lee MR. Treatment of Alcohol Use Disorder in Patients with Alcoholic Liver Disease. Am J Med. 2017;130(2):124–34. doi: 10.1016/j.amjmed.2016.10.004
43. Halpin LE, Gunning WT, Yamamoto BK. Methamphetamine causes acute hyperthermia-dependent liver damage. Pharmacol Res Perspect. 2013;1(1):1–11. doi: 10.1002/prp2.8.
44. Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Lancet Glob Heal. 2017;5(12):e1192–207. doi: 10.1016/S2214-109X(17)30375-3
45. United Nations on Drug and Crime (UNODC). World Drug Report 2017 [Internet]. [cited 2020 May 6]. Available from: https://www.unodc.org/wdr2017/index.html.

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