Rev Esp Nutr Hum Diet. 2021; 25(2).
doi: 10.14306/renhyd.25.2.1157 [ahead of print]

Freely available online - OPEN ACCESS

Revista Española de Nutrición Humana y Dietética

Spanish Journal of Human Nutrition and Dietetics

RESEARCH – *post-print* version

This is the accepted peer-reviewed version for publication. The article can receive style and format modifications.

Drug abuse and serum nutritional biomarkers: A retrospective cohort study

Abuso de drogas y biomarcadores séricos nutricionales: Un estudio retrospectivo de cohorte

Alfonso Daniel Silva Ochoa[a], José Alejandro Valdevila Figueira[b], Rocío Valdevila Santiesteban[c], Diego Javier Estrella Almeida[b,*], Luz Maria Valencia Erazo[a], Andrea Katherine Orellana Manzano[a].

[a] Laboratorio para Investigaciones Biomédicas, Facultad de Ciencias de la Vida, Escuela Superior Politécnica del Litoral, Guayaquil, Ecuador.
[b] Instituto de Neurociencias, Guayaquil, Ecuador.
[c] Universidad de Ciencias Médicas, Holguín, Cuba.
* djeadiego@hotmail.com

Received: 09/29/2020; accepted: 01/24/2021; Posted: 02/03/2021

CITA: Silva Ochoa AD, Valdevila Figueira JA, Valdevila Santiesteban R, Estrella Almeida DJ, Valencia Erazo LM, Orellana Manzano AK. Drug abuse and serum nutritional biomarkers: A retrospective cohort study. Rev Esp Nutr Hum Diet. 2021; 25(2). doi: 10.14306/renhyd.25.2.1157 [ahead of print]

ABSTRACT

Introduction: Drug abuse is a public health problem around the globe. Its implications in human health are harmful, compromising nutritional status. It has been shown that malnutrition is moderately prevalent in drug addicts, and a nutritional prescription is significantly beneficial for these patients. Available literature suggests altered blood serum biochemical data in drug addicts. Our study focused on blood serum nutritional biomarkers in drug addicts who did not have a nutritional assessment or treatment. This study aimed to analyze nutritional blood serum biomarkers in subjects diagnosed with drug addiction from January 2010 to June 2020.

Methods: The research was a retrospective cohort, analytical, observational, and was based on a convenience sample. Data about blood serum AST, ALT, fasting glucose, urea, creatinine, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and hemoglobin were analyzed from a database of 103 subjects diagnosed with mental and behavioral disorders due to the use of drugs and other psychoactive substances (ICD-10: F10-F19) in the Institute of Neurosciences (INC). Consumed drugs were alcohol, cocaine, amphetamines, MDNA, opioids, marijuana, and psychotropic drugs.

Results: The medians of hemoglobin, total cholesterol, HDL, and creatinine statistically differed between genders and age groups. There were more cases of low blood hemoglobin and hyperglycemia levels in men, (20.4, and 8.7%, respectively) than women (4.9%, and 0%, respectively). There were low levels of fasting glucose in 8.8% of our sample. Serum creatinine levels were significantly increased in subjects aged 30 or more.

Conclusions: In our sample, there were statistically different medians of hemoglobin, total cholesterol, HDL, and creatinine among groups of gender and age in drug addicts. All medians were within the normal range.

Keywords: Substance-Related Disorders; Alcoholism; Marijuana Abuse; Amphetamine-Related Disorders; Opioid-Related Disorders; Cocaine-Related Disorders; Transaminases; Erythrocyte Indices; Creatinine; *Drug abuse*.

RESUMEN

Introducción: El abuso de drogas es un problema de salud pública en todo el mundo. Sus implicaciones en la salud humana son nocivas y comprometen el estado nutricional. Se ha demostrado que la desnutrición tiene una prevalencia moderada en los drogadictos y una prescripción nutricional es significativamente beneficiosa para estos pacientes. La literatura disponible sugiere datos bioquímicos de suero sanguíneo alterados en adictos a las drogas. Nuestro estudio se centró en los biomarcadores nutricionales del suero sanguíneo en adictos a las drogas que no tenían una evaluación o tratamiento nutricional. Este estudio tuvo como objetivo analizar los biomarcadores nutricionales del suero sanguíneo en sujetos diagnosticados con adicción a las drogas desde enero de 2010 hasta junio de 2020.

Material y métodos: La investigación fue de cohorte retrospectiva, analítica, observacional y se basó en una muestra de conveniencia. Los datos sobre AST, ALT, glucosa en ayunas, urea, creatinina, colesterol total, colesterol HDL, colesterol LDL, triglicéridos y hemoglobina en suero sanguíneo se analizaron a partir de una base de datos de 103 sujetos diagnosticados con trastornos mentales y del comportamiento debido al uso de drogas y otros sustancias psicoactivas (CIE-10: F10-F19) en el Instituto de Neurociencias (INC). Las drogas consumidas fueron alcohol, cocaína, anfetaminas, MDNA, opioides, marihuana y drogas psicotrópicas.

Resultados: Las medianas de hemoglobina, colesterol total, HDL y creatinina difirieron estadísticamente entre sexos y grupos de edad. Hubo más casos de niveles bajos de hemoglobina en sangre e hiperglucemia en hombres (20,4 y 8,7%, respectivamente) que en mujeres (4,9% y 0%, respectivamente). Hubo niveles bajos de glucosa en ayunas en el 8,8% de nuestra muestra. Los niveles de creatinina sérica aumentaron significativamente en sujetos de 30 años o más.

Conclusiones: En nuestra muestra, hubo medianas estadísticamente diferentes de hemoglobina, colesterol total, HDL y creatinina entre grupos de sexo y edad en drogadictos. Todas las medianas estaban dentro del rango normal.

Palabras clave: Trastornos Relacionados con Sustancias; Alcoholismo; Abuso de Marihuana; Trastornos Relacionados con Anfetaminas; Trastornos Relacionados con Opioides; Trastornos Relacionados con Cocaína; Transaminasas; Índices de Eritrocitos; Creatinina; *Abuso de drogas*.

KEY MESSAGES

INTRODUCTION

Addiction is commonly identified with nonmedical self-administration of drugs, and it is usually defined by characteristics of intoxication or by characteristics of withdrawal symptoms (1). Understanding of drug addiction has perhaps made the most progress when conceived in terms of its underlying neuropsychological processes (2). Classic ideas of Pavlovian conditioning, positive reinforcement, opponent motivational processes, and cognitive control have all been shown to play a role not only in explaining bizarre behavioral symptoms of drug addicts, but also in relating the behavior to underlying dysfunctional neural networks(3).

Facets other than pharmacological therapy include treatment for withdrawal or addiction, nutrition support, and potential for transmission of infectious diseases(4). Nutrition education contributes to changes in eating environments to facilitate dietary behavior changes in community residential substance-abuse settings(5).

Drug abuse and blood serum biomarkers

There are some neurobehavioral similarities between appetites for drugs and foods(6). There is a relationship between imbalances due to diet and substance use(7). Although the relationship between alcohol intake and overweight development is highly controversial, some possible mechanisms responsible for this effect are an addition to energy from other sources due to heavy drinking or binge drinking, little effect on satiety, possible influence over energy intake by inhibiting the effects of leptin, or glucagon-like peptide-1 (GLP-1) and increasing cholecystokinin, the primary use of alcohol for heat production, and lifestyle of subjects(8). Research on ghrelin's role in alcoholism/alcohol use disorder (AUD) in general present evidence that the ghrelin system seems to activate the mesolimbic dopaminergic system via its GHS-R1A receptor and ghrelin receptor antagonists attenuate activity within this system(9). Ghrelin receptor antagonists may be of use in reducing craving and alcohol consumption, or in promoting long-term abstinence following detoxification(10). However, the administration of such agents would be expected to lead to significant weight loss if used chronically(10). A study with patients undergoing alcohol and drug treatment found a high level of micronutrient malnutrition (mainly vitamin A, iron, and potassium) and risk related to a poor appetite and diet quality. Moreover, 81% of all participants were at significant risk of future weight loss owing to a poor appetite, and the prevalence of moderate malnutrition according to the Subjective Global Assessment (SGA) was 24%(11).

Cannabis has been used since ancient times to relieve neuropathic pain, lower intraocular pressure, increase appetite, and decrease nausea and vomiting(12–14). Recent studies in humans show that, in addition to absolute amounts of omega-6 and omega-3, fatty acid intake, a higher omega-6/omega-3 ratio plays an important role in increasing the development of obesity via both arachidonic acid eicosanoid metabolites and hyperactivity of the cannabinoid system(15). However, a meta-analysis revealed significantly reduced body mass index and rates of obesity in Cannabis users, in conjunction with increased caloric intake, by rapid and long-lasting downregulation of CB1R following acute Cannabis consumption that reduces energy storage and increases metabolic rates(16).

Excessive salt intake is related to high blood pressure in humans. Opioid signaling powerfully influences multiple components of the circuitry incentive salience for salt, and further characterizing these roles is important for human health(17). Regarding pregnant women, lower body mass index and folate, B12, and iron deficiencies were found in women with opioid use disorder (OUD) compared with women without OUD(18).

Amphetamines suppress appetite by increasing the synaptic availabilities of norepinephrine and dopamine in the hypothalamus and subsequently activates the norepinephrine - and dopamine-dependent mechanisms that attenuate the central nervous system control of food intake(19). In addition to the catecholamine effects, recent studies have reported that the interaction between hypothalamic dopamine and neuropeptide Y (NPY), an orexigenic neuropeptide, plays a key role in the anorectic effect of amphetamines(20). A systematic review including overweight and obese adults with binge-eating disorder found that lisdexamfetamine reduced weight and appetite(21).

Cocaine, a serotonin-norepinephrine-dopamine reuptake inhibitor that serves as an illegal stimulant, appetite suppressant, and anesthetic, also causes vasoconstriction and rhabdomyolysis(22). One reason for its effect as an appetite suppressant could be that sigma-1 receptor (σ1R) mediates cocaine anorectic effects by interacting in neurons with growth/hormone/secretagogue (ghrelin) receptors. On the other hand, cocaine use has been related to excessive body weight gain when individuals enter treatment and stop using it. Chronic cocaine exposure may enhance food consumption by modulating 5-HT neurotransmission in the arcuate nucleus directly via SERT inhibition, and indirectly by reducing leptin production through its peripheral effects. The specific appetite for fat may, however, be modulated by cocaine's excitatory effects on the hypothalamic-pituitary-adrenal axis (HPA) through the release of hypothalamic corticotropin-releasing factor (CRF)(23).

Macronutrients increase the odds of substance use and micronutrients decrease the odds of substance use, especially among females. Besides, the nutrient imbalance is a particularly strong predictor of substance use for both males and females(24). Dilutional hyponatremia is mainly caused by direct stimulation of antidiuretic hormone (ADH) secretion by ecstasy (MDMA). Females using ecstasy could be at increased risk of developing severe hyponatremia than males(25).

Malnutrition is a major consequence due to substances replacing nutrients and interfering with their metabolism(26) and is related to complications in wound healing and infections(27). Subjects with substance use disorder could present a significant deficiency of serum folic acid and B12 levels(28). Low blood levels of folic acid and B12 could result in anemia characterized by fatigue, loss of energy, dizziness, tachycardia, and conjunctival pallor.

Overweight and obesity promote chronic low-grade inflammation due to an adipokines synthesis increase (TNFα, IL-6, MCP-1, and resistin), which can cause harm kidneys, liver, pancreas, and heart. Abnormal blood serum parameters can suggest disturbances in the homeostasis of such body organs(29).

Poor nutritional status in AUD and drug use disorder (DUD) severely impacts their physical and psychological health, which may impede their ability to resist substances of abuse and recover their health(30).

As described above, malnutrition-related alterations result in interactions between body organs' functionality and biological processes that would be evidenced in biochemical parameters. Moreover, blood serum biochemical data are used to complement the assessment of nutritional status. Small improvements in the nutritional environment may translate to large gains in mental health and wellbeing at a population level(4).

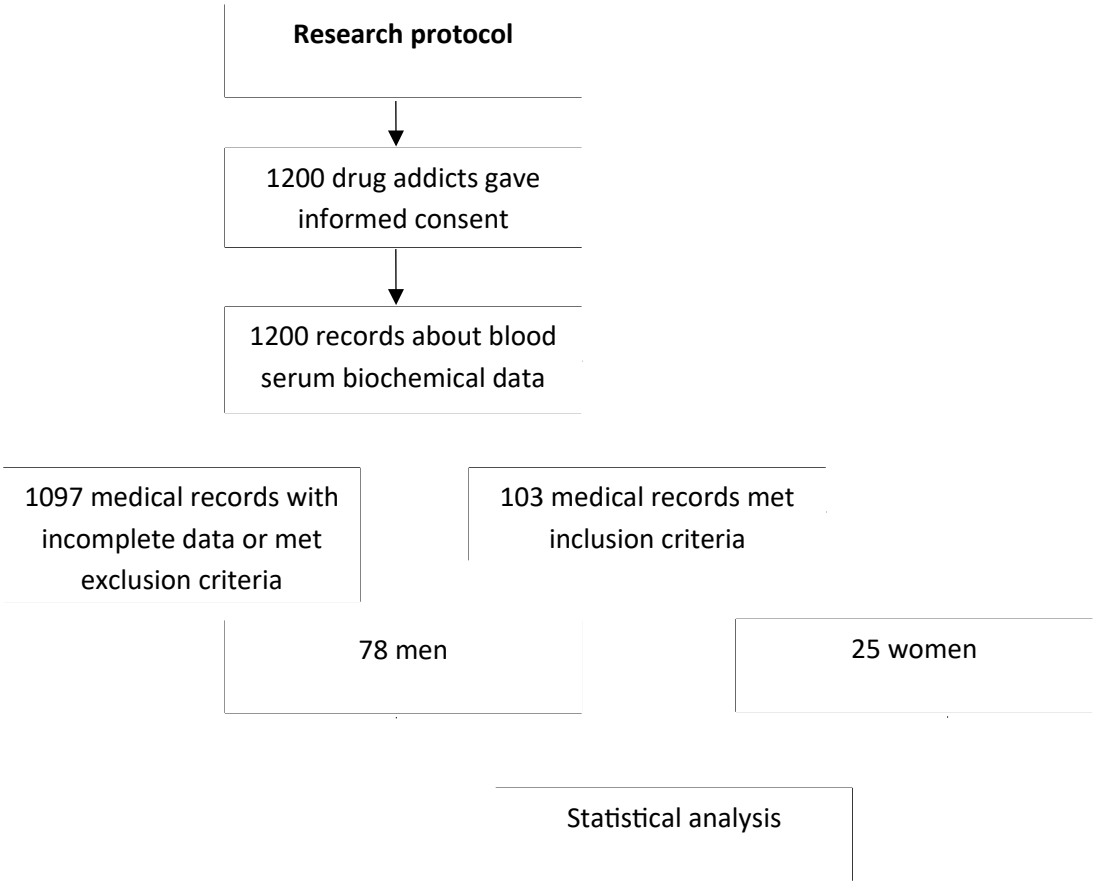
Senescence is characterized by a decline in renal and liver functions; however, this decline could begin from adulthood depending on childhood lifestyle. Some factors could promote such a decline as unhealthy food intake, chronic diseases, pathogens, and drug abuse. It is known that cocaine and marijuana could promote renal and liver damage. Therefore, this study aimed to analyze nutritional serum biomarkers in subjects diagnosed with drug addiction from January 2010 to June 2020.

MATERIAL AND METHODS

Study design and biochemical parameters

The research was a retrospective cohort, analytical, observational, and was based on a convenience sample. Information about blood serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), fasting glucose, urea, creatinine, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, and hemoglobin were analyzed from a database of 103 subjects from the Institute of Neurosciences of Guayaquil (INC). Reference ranges for blood tests from the INC (See Table AM1 in additional materials: http://www.renhyd.org/index.php/renhyd/article/view/1157/743) were considered. Each blood test was carried out during the first week of admission to the INC in the absence of symptoms related to acute toxicity or abstinence syndrome, and with negative rapid tests for drugs (cocaine, amphetamines, 3,4-methylenedioxymethamphetamine (MDNA), opioids, marijuana, and psychotropic drugs). Patients were admitted to the drug addiction rehabilitation program from the Addictive Behavior Unit (UCA) from the INC from January 2010 to June 2020. Inclusion criteria involved informed consent, age between 18 and 67 years, and clinical history of chronic abuse of alcohol, marijuana, amphetamines, opioids, and cocaine (hydrochloride, base, and crack). Exclusion criteria involved the presence of chronic diseases (liver, kidney, and pancreas) that limit compliance with the research program diagnosed by medical examination and laboratory tests. Subjects were under medical treatment. No sensitive personal information was included, analyzed, or distributed. Subjects submitted informed consent, and the INC supported the research protocol. In the beginning, we wanted to compare serum nutritional biomarkers between adults and the elderly, but we had a very limited number of older adults. Considering that these groups are highly uneven, we determined that the best way to solve this issue was to divide our sample into two even groups (age <30 and ≥30).

Figure 1. Study design.



Statistical analyses

Descriptive characteristics of nutritional biomarkers in our sample were expressed as medians with interquartile ranges, and percentages for quantitative and categorical variables, respectively. The normality was analyzed with the Kolmogorov-Smirnov test. Mann–Whitney U test was applied to determine significant differences among medians of the groups (gender and ages <30 and ≥30). Fisher's exact test was used to determine significant differences between the percentages of abnormal blood serum biomarkers and genders. Analyses were adjusted for confounding factors including gender and age when these were not the exposure. The group difference was considered statistically significant for $p < 0.05$. There were 1097 uncomplete medical records because 4 years ago there was no admission protocol requesting all laboratory tests included in this research. However, missing data were not included in the statistical analysis. All data were analyzed with RStudio version 1.3.1073.

RESULTS

Nutritional serum markers

The hemoglobin median was significantly higher in men than women and was found within the normal range in both genders (Table 1). However, we found more cases of low blood hemoglobin levels in men (20.4%) than in women (4.9%) (Table 2). The glucose median was found within the normal range for both genders and the difference was not statistically significant (Table 1). The prevalence of abnormal values regarding blood glucose in genders differed significantly (Table 2). HDL values were significantly higher in women than in men. In contrast, the median creatinine was significantly higher in men than in women (Table 1). On the other hand, hemoglobin and HDL were within normal range parameters. In subjects aged 30 or more, we observed a significant increase in the medians of total cholesterol, and creatinine (Table 1). Reference ranges can be found in Table AM1 in additional materials.

Table 1. Median of nutritional serum markers by gender and age.

Nutritional serum biomarkers (n=103)	**Men Median (IQR)**	**Women Median (IQR)**	***p-value***	**<30 yo Median (IQR)**	**≥30 yo Median (IQR)**	***p-value***
Hemoglobin (g/dL)	14.30 (13.63 to 15.05)	12.90 (12.20 to 13.80)	<0.001 ***	14 (13.30 to 14.90)	14.1 (12.98 to 14.83)	0.710
Glucose (mg/dL)	84 (77 to 89)	79 (74 to 88)	0.099	84 (75 to 87.5)	82 (76 to 90.0)	0.836
Total Cholesterol (mg/dL)	167.5 (147.25 to 195.75)	173 (155 to 216)	0.276	157 (143 to 190.50)	183.5 (151.75 to 205.25)	0.044*
LDL (mg/dL)	95.05 (74.7 to 116)	106 (79.0 to 131)	0.185	95 (71.50 to 110)	99.4 (82.75 to 123.93)	0.238
HDL (mg/dL)	42 (35 to 50)	56 (42 to 63)	<0.001 ***	46 (37 to 57)	44 (35.75 to 51)	0.226
Creatinine (mg/dL)	0.930 (0.833 to 1.088)	0.730 (0.650 to 0.950)	<0.001 ***	0.89 (0.76 to 0.95)	0.935 (0.81 to 1.14)	0.029*

Statistical significance *** p <0.001, ** p <0.01, * p <0.05. **n**: Sample Size. **LDL**: Low Density Lipid. **HDL**: High Density Lipid. **IQR**: Interquartile range. **yo**: years old. Mann–Whitney U test was applied to determine significant differences among medians of the groups. None of the medians was found outside the reference values. Serum hemoglobin, total cholesterol, HDL and creatinine were significantly different among groups.

Table 2. Percentages of nutritional serum markers levels by gender.

Biochemical parameters	PERCENTAGE (%)			
	High	Low	Normal	Fisher's Exact Test *p*-value
Hemoglobin				
Men	-	20.4	55.3	0.602
Women	-	4.9	19.4	
Glucose				
Men	8.7	3.9	63.1	0.023*
Women	0.0	4.9	19.4	
Total cholesterol				
men	7.8	-	68	0.479
women	3.9	-	20.4	
LDL				
men	1.9	-	73.8	0.091
women	2.9	-	21.4	
HDL				
men	-	31.1	44.7	0.029*
women	-	3.9	20.4	
Triglycerides				
men	19.4	-	56.3	0.021*
women	1	-	23.3	
Creatinine				
men	8.7	0.0	67.0	0.343
women	1.9	1	21.4	
Urea				
men	9.7	0.0	66.0	0.227
women	1.9	1	21.4	
AST				
men	12.6	-	63.1	0.755
women	2.9	-	21.4	
ALT				
men	14.6	-	61.2	0.551
women	2.9	-	21.4	
Statistical significance* ** p <0.001, ** ** p <0.01, * p <0.05. **LDL**: Low Density Lipid. **HDL**: High Density Lipid. **AST**: Aspartate Aminotransferase. **ALT**: Alanine Aminotransferase. Fisher's Exact Test was applied to determine associations between genders and percentages. According to our results, we would expect more men experiencing abnormal glucose, triglycerides, and HDL blood levels than women.				

Men presented higher percentages of high serum levels of total cholesterol, LDL, and triglycerides (7.8, 1.9, and 19.4%, respectively) than women (3.9, 2.9, and 1%, respectively). However, only the percentages regarding categorical variables (high, normal, or low blood levels) of glucose, HDL, and triglycerides were statistically significant (Table 2).

Kidney and liver serum markers

Regarding high levels of creatinine, urea, AST, and ALT, the total sample showed 10.6%, 11.6%, 15.5%, and 17.5%, respectively. Men had a higher prevalence of abnormal levels of these biomarkers compared to women, but such percentages were not statistically different (Table 2).

Despite all these differences in blood serum values between men and women, none of the medians were found outside the reference ranges (Table 1). Reference ranges are in Table AM1 in additional materials.

DISCUSSION

In this study, abnormal levels in kidney and liver biomarkers, hemoglobin, glucose, and lipids were found in our subjects. However, their medians were found within reference ranges. In drug addicts, we will probably find more men and people aged more than 30 experiencing dyslipidemia and diseases related to kidneys and liver compared to women and people aged less than 30.

According to the INC, the most common admission diagnosis is opiates drug addiction(heroin type). In crack cocaine users, Escobar et al. found hemoglobin and hematocrit levels below normal for 32.4 and 30.6% of patients, respectively(31). Considering normal parameters, a large part of the sample (60.2%) had low levels of HDL cholesterol and high levels of triglycerides (38%)(31). We found similar values for low hemoglobin levels and high levels of triglycerides (25.3 and 20.4%, respectively). 35% of our sample presented low HDL levels. Iron and hemoglobin metabolism are tightly related to the kidneys. Kidneys are responsible for the erythropoietin synthesis, which promotes de novo red blood cells from the bone marrow(32). Any renal harm may result in anemia, including harm from drug abuse. Other factors that could promote anemia are subclinical or undiagnosed diseases, food insecurity, poverty, and difficult living conditions(33). As described in the introduction, once individuals enter treatment and stop using cocaine, their appetite (affected by chronic cocaine use) could encourage excessive calorie consumption. Furthermore, without nutritional counseling, this excessive energy intake could explain the moderate prevalence of dyslipidemia in our sample. In one study, cocaine users reported significantly higher levels of dietary fat and carbohydrates as well as patterns of uncontrolled eating, and their fat mass was significantly reduced compared with their non-drug using peers(34). Although our study did not show this data, future research should explore more deeply chronic cocaine use, recovery periods, and endogenous nutrients metabolism.

According to Zhang Y et al., Zhang M et al., and Lv et al., methamphetamine abuse in humans induces a significant decrease in fasting blood glucose(35–37). We found low levels of fasting glucose in 8.8% of our sample. Even though we did not include subjects with diabetes, it can be highlighted that the effect of substance abuse on glycated hemoglobin and postprandial blood glucose in patients with diabetes was not significant in a review by Ojo et al(38). However, while the value was slightly lower concerning postprandial blood glucose, this was slightly higher in relation to glycated hemoglobin (HbA1c) in the substance abuse group compared with control. On the other hand, the effect of substance

abuse on fasting blood glucose was significant ($p = 0.03$) compared with control, but this was attenuated following a sensitivity test. This would suggest that substance abuse on fasting blood glucose is not very reliable or transient. A range of factors, including narcotic withdrawal, intercurrent infections, eating habits, characteristics of drugs, and patients' erratic lifestyle, may explain the outcome(38). Drug abuse increases the risk of hypoglycemia, compounded by erratic dietary habits(39). Studies in humans and a variety of preclinical models indicate that acute administration of alcohol can lead to either a reduction or no change in the circulating concentration of glucose. However, hypoglycemia would only be anticipated in humans with AUD who also have a relatively poor nutritional status or severely impaired liver function(40). However, another study considering that moderate alcohol intake may increase the risk of type 2 diabetes, found that one-week alcohol abstinence improved hepatic insulin sensitivity and fasting plasma glucose in non-obese Japanese men with mildly elevated fasting plasma glucose and drinking habits alcohol(41). Therefore, it could be interesting to explore these biomarkers on subjects with chronic diseases and drug abuse.

Zhang et al. found that ALT, creatine kinase, and creatinine biochemical serum values in humans were significantly increased in the methamphetamine group. Serum calcium and albumin were found to be significantly decreased in the methamphetamine group(35). However, Lu et al. did not observe any clinically significant association between current or past self-reported marijuana use and measures of kidney function(42). In our sample, the high levels of serum ALT, AST, and creatinine corresponded to 17.5, 15.5, and 10.6%, respectively. Anabolic androgenic steroids, synthetic cannabinoids (also known as "Spice" or "K2"), ecstasy (formally known as MDMA), and cocaine and its levamisole-adulterated counterpart are common or emerging drugs of abuse with severe nephrotoxic effects about which both the community and health care providers should become more aware(22). Levamisole has been increasingly used as an adulterant of cocaine in recent years, emerging as a public health challenge worldwide and its toxicity manifests clinically as systemic vasculitis, consisting of cutaneous, hematological, and renal lesions(43). An estimated one-third of individuals with a history of opioid misuse or addiction are thought to have AUD regarding the liver. Additionally, opioids may also directly contribute to or exacerbate liver disease because some opioids are metabolized in the liver via the P450 system, and it has been shown and elevation in biochemical markers, particularly alanine aminotransferase, lactate dehydrogenase, and lipid peroxides among chronic heroin users thus suggesting direct hepatotoxic effects(44). Studies relating to cannabis use and liver

health remain unclear. While some studies have suggested possible associations between cannabis consumption and hepatomegaly, others have suggested a decreased prevalence of nonalcoholic fatty liver disease (NAFLD), and significantly lower odds of developing steatosis, steatohepatitis, cirrhosis, and hepatocellular carcinoma in alcohol abusers who also used marijuana. Possible negative effects on the liver could be due to underlying viral infections, which are common among marijuana users. Furthermore, four cases of hepatic failure associated with cannabis or its synthetic analogs have been reported in the literature(45).

Zhang M et al. observed significant decreases in total cholesterol and triglycerides in methamphetamine-dependent patients compared to the control group(36). Our study was observational, not experimental. Thus, we are limited to specify that we did not observe low serum levels of total cholesterol and triglycerides. 11.7 and 20.4% of our sample showed high levels of cholesterol and triglycerides, respectively. Differences in body composition could explain statistically significant differences regarding medians and genders. It is known that men have more muscle and less adipose tissue than women, and this condition could result in higher levels of hemoglobin and creatinine. However, high levels of serum creatinine could suggest kidney disease. HDL increase in women compared to men could be explained by their complex lipid metabolism due to hormones, breastfeeding, and preparation for pregnancy in the future. People aged 30 or more had significantly higher levels of serum creatinine, possibly suggesting initial stages of kidney disease. As described in the introduction, organs functions decline with age. Their different lifestyles and conditions could explain statistically significant differences regarding the prevalence of abnormal serum biomarkers between genders.

The drug addiction treatment from INC is designed in 3 components. Such components are "general services" that includes meals, hygiene, and nursing care; "psychotherapy program" that includes individual therapy, group therapy, crisis intervention, family and multifamily therapy, a quality-of-life program for physical exercise training, and social and recreational skills development through healthy use of free time; and "occupational therapy and pharmacotherapy" carried out according to individual needs.

Nutrition services are not part of the 3 components described above. Nonetheless, nutrition plays a key role in the treatment of drug addicts. Nutrition services should be implemented to screen for nutritional risks daily. This will help to determine which patients are at high risk for undernutrition and thus, rapidly implement nutrition care. A good nutritional status will promote life expectancy and quality.

The study limitations involve lack of monitoring of prescribed medicines consumption in follow-up consultations, lack of nutritional counseling because there are no dietitians in the INC, and 4 years ago there was no admission protocol requesting all laboratory tests included in this research. Some feasible confounding factors would be a lack of deep analysis of food insecurity, poverty, and difficult living conditions among subjects. These could be confounding factors because they can decrease food intake, resulting in abnormal blood serum nutritional biomarkers.

CONCLUSIONS

There were statistically different medians of hemoglobin, total cholesterol, HDL, and creatinine among groups of gender and age in drug addicts in our sample. All medians were within the normal range. Considerably high percentages of low levels of hemoglobin, HDL, and high levels of total cholesterol, triglycerides, LDL, and liver enzymes were observed in men. Healthcare professionals should closely monitor red blood cells, blood lipids, kidneys, and liver status in this population. Further studies exploring the relationship between drug abuse and nutritional status are needed.

AUTHORS' CONTRIBUTIONS

ADSO: Drafting and statistical analysis. JAVF: Preparation of database, collection of biological samples and review of the article. RVS: Database development, collection and analysis of biological samples. DJEA: Review of the article and elaboration of the database. LMVE: Review of the article and statistical analysis. AKOM: Review of the article and statistical analysis.

FUNDING

The authors have no financial relationships relevant to this article to disclose.

COMPETING INTERESTS

The authors state that there are no conflicts of interest in preparing the manuscript.

REFERENCES

(1) Wise RA, Robble MA. Dopamine and Addiction. Annu Rev Psychol. 2020;71(1):79–106, doi: 10.1146/annurev-psych-010418-103337

(2) Understanding Drug Use and Addiction DrugFacts | National Institute on Drug Abuse (NIDA) [Internet]. [cited 2020 Dec 22]. Available from: https://www.drugabuse.gov/publications/drugfacts/understanding-drug-use-addiction

(3) Everitt BJ, Robbins TW. Drug Addiction: Updating Actions to Habits to Compulsions Ten Years On. Annu Rev Psychol. 2016;67(1):23–50, doi: 10.1146/annurev-psych-122414-033457

(4) Rech MA, Donahey E, Cappiello Dziedzic JM, Oh L, Greenhalgh E. New Drugs of Abuse. Pharmacother J Hum Pharmacol Drug Ther. 2015;35(2):189–97. doi: 10.1002/phar.1522

(5) Cowan JA, Devine CM. Process evaluation of an environmental and educational nutrition intervention in residential drug-treatment facilities. Public Health Nutr. 2012;15(7):1159-67, doi: 10.1017/S1368980012000572.

(6) Rogers PJ. Food and drug addictions: Similarities and differences. Pharmacol Biochem Behav. 2017;153:182-90, doi: 10.1016/j.pbb.2017.01.001.

(7) Jack HE, Oller D, Kelly J, Magidson JF, Wakeman SE. Addressing substance use disorder in primary care: The role, integration, and impact of recovery coaches. Subst Abus. 2018;39(3):307-14, doi: 10.1080/08897077.2017.1389802

(8) Jack HE, Oller D, Kelly J, Magidson JF, Wakeman SE Addressing substance use disorder in primary care: The role, integration, and impact of recovery coaches. Subst Abus. 2018;39(3):307-14, doi: 10.1080/08897077.2017.1389802.

(9) Zallar LJ, Farokhnia M, Tunstall BJ, Vendruscolo LF, Leggio L. The Role of the Ghrelin System in Drug Addiction. In: International Review of Neurobiology. Academic Press Inc.; 2017. p. 89–119.

(10) Koopmann A, Schuster R, Kiefer F. The impact of the appetite-regulating, orexigenic peptide ghrelin on alcohol use disorders: A systematic review of preclinical and clinical data. Biol Psychol. 2018;131:14-30, doi: 10.1016/j.biopsycho.2016.12.012.

(11) Ross LJ, Wilson M, Banks M, Rezannah F, Daglish M. Prevalence of malnutrition and nutritional risk factors in patients undergoing alcohol and drug treatment. Nutrition. 2012;28(7-8):738-43, doi: 10.1016/j.nut.2011.11.003.

(12) Pacifici R, Marchei E, Salvatore F, Guandalini L, Busardò FP, Pichini S. Evaluation of cannabinoids concentration and stability in standardized preparations of cannabis tea and cannabis oil by ultra-high performance liquid chromatography tandem mass spectrometry. Clin Chem Lab Med. 2017;55(10):1555-63, doi: 10.1515/cclm-2016-1060.

(13) Fraguas-Sánchez AI, Torres-Suárez AI. Medical Use of Cannabinoids. Drugs. 2018;78(16):1665-703, doi: 10.1007/s40265-018-0996-1.

(14) Hoffenberg EJ, McWilliams S, Mikulich-Gilbertson S, Murphy B, Hoffenberg A, Hopfer CJ. Cannabis Oil Use by Adolescents and Young Adults With Inflammatory Bowel Disease. J Pediatr Gastroenterol Nutr. 2019;68(3):348-52, doi: 10.1097/MPG.0000000000002189.

(15) Simopoulos AP. An Increase in the Omega-6/Omega-3 Fatty Acid Ratio Increases the Risk for Obesity. Nutrients. 2016;8(3):128, doi: 10.3390/nu8030128.

(16) Clark TM, Jones JM, Hall AG, Tabner SA, Kmiec RL. Theoretical Explanation for Reduced Body Mass Index and Obesity Rates in Cannabis Users. Cannabis Cannabinoid Res. 2018;3(1):259-71, doi: 10.1089/can.2018.0045.

(17) Smith CM, Lawrence AJ. Salt Appetite, and the Influence of Opioids. Neurochem Res. 2018;43(1):12-8, doi: 10.1007/s11064-017-2336-3.

(18) Nagarajan MK, Goodman D. Not just substance use: the critical gap in nutritional interventions for pregnant women with opioid use disorders. Public Health. 2020;180:114-6, doi: 10.1016/j.puhe.2019.10.025.

(19) Volkow ND, Wise RA, Baler R. The dopamine motive system: implications for drug and food addiction. Nat Rev Neurosci. 2017;18(12):741-52, doi: 10.1038/nrn.2017.130.

(20) Lemieux AM, Li B, al'Absi M. Khat use and appetite: an overview and comparison of amphetamine, khat and cathinone. J Ethnopharmacol. 2015;160:78-85, doi: 10.1016/j.jep.2014.11.002.

(21) Brownley KA, Berkman ND, Peat CM, Lohr KN, Cullen KE, Bann CM, et al. Binge-Eating Disorder in Adults: A Systematic Review and Meta-analysis. Ann Intern Med. 2016;165(6):409-20, doi: 10.7326/M15-2455.

(22) Pendergraft WF, Herlitz LC, Thornley-Brown D, Rosner M, Niles JL Nephrotoxic effects of common and emerging drugs of abuse. Clin J Am Soc Nephrol. 2014;9(11):1996-2005, doi: 10.2215/CJN.00360114.

(23) Billing L, Ersche KD. Cocaine's appetite for fat and the consequences on body weight. Am J Drug Alcohol Abuse. 2015;41(2):115-8, doi: 10.3109/00952990.2014.966196.

(24) Schroeder RD, Higgins GE. You Are What You Eat: The Impact of Nutrition on Alcohol and Drug Use. Subst Use Misuse. 2017;52(1):10-24, doi: 10.1080/10826084.2016.1212603.

(25) van Dijken GD, Blom RE, Hené RJ, Boer WH, NIGRAM Consortium. High incidence of mild hyponatraemia in females using ecstasy at a rave party. Nephrol Dial Transplant. 2013;28(9):2277-83, doi: 10.1093/ndt/gft023.

(26) Cunningham PM. The Use of Sobriety Nutritional Therapy in the Treatment of Opioid Addiction. J Addict Res Ther. 2016;7(3), doi: 10.4172/2155-6105.1000282.

(27) Saeland M, Wandel M, Böhmer T, Haugen M. Abscess infections and malnutrition--a cross-sectional study of polydrug addicts in Oslo, Norway. Scand J Clin Lab Invest. 2014;74(4):322-8, doi: 10.3109/00365513.2014.891256.

(28) Yazici AB, Akcay Ciner O, Yazici E, Cilli AS, Dogan B, Erol A. Comparison of vitamin B12, vitamin D and folic acid blood levels in patients with schizophrenia, drug addiction and controls. J Clin Neurosci. 2019;65:11-6, doi: 10.1016/j.jocn.2019.04.031.

(29) Guzik TJ, Skiba DS, Touyz RM, Harrison DG. The role of infiltrating immune cells in dysfunctional adipose tissue. Vol. 113, Cardiovascular Research. Oxford University Press; 2017 [cited 2020 Dec 22]. p. 1009–23. Available from: https://academic.oup.com/cardiovascres/article/113/9/1009/3952694

(30) Jeynes KD, Gibson EL. The importance of nutrition in aiding recovery from substance use disorders: A review. Drug Alcohol Depend. 2017;179:229-39, doi: 10.1016/j.drugalcdep.2017.07.006.

(31) Escobar M, Scherer JN, Soares CM, Guimarães LSP, Hagen ME, von Diemen L, et al. Active Brazilian crack cocaine users: nutritional, anthropometric, and drug use profiles. Braz J Psychiatry. 2018;40(4):354-60, doi: 10.1590/1516-4446-2017-2409.

(32) Gafter-Gvili A, Schechter A, Rozen-Zvi B. Iron Deficiency Anemia in Chronic Kidney Disease. Acta Haematol. 2019;142(1):44-50, doi: 10.1159/000496492.

(33) Harding KL, Aguayo VM, Namirembe G, Webb P. Determinants of anemia among women and children in Nepal and Pakistan: An analysis of recent national survey data. Matern Child Nutr. 2018;14 Suppl 4:e12478, doi: 10.1111/mcn.12478.

(34) Ersche KD, Stochl J, Woodward JM, Fletcher PC. The skinny on cocaine: insights into eating behavior and body weight in cocaine-dependent men. Appetite. 2013;71:75-80, doi: 10.1016/j.appet.2013.07.011.

(35) Zhang Y, Shu G, Bai Y, Chao J, Chen X, Yao H. Effect of methamphetamine on the fasting blood glucose in methamphetamine abusers. Metab Brain Dis. 2018;33(5):1585-97, doi: 10.1007/s11011-018-0265-8.

(36) Zhang M, Lv D, Zhou W, Ji L, Zhou B, Chen H, et al. The levels of triglyceride and total cholesterol in methamphetamine dependence. Medicine (Baltimore). 2017;96(16):e6631, doi: 10.1097/MD.0000000000006631.

(37) Lv D, Zhang M, Jin X, Zhao J, Han B, Su H, et al. The Body Mass Index, Blood Pressure, and Fasting Blood Glucose in Patients With Methamphetamine Dependence. Medicine (Baltimore). 2016;95(12):e3152, doi: 10.1097/MD.0000000000003152.

(38) Ojo O, Wang X-H, Ojo OO, Ibe J. The Effects of Substance Abuse on Blood Glucose Parameters in Patients with Diabetes: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2018;15(12), doi: 10.3390/ijerph15122691.

(39) Singh Balhara YP, Kalra S. Drug addiction and diabetes: South Asian action. J Pak Med Assoc. 2017;67(6):954-6.

(40) Steiner JL, Crowell KT, Lang CH. Impact of Alcohol on Glycemic Control and Insulin Action. Biomolecules. 2015;5(4):2223-46, doi: 10.3390/biom5042223.

(41) Funayama T, Tamura Y, Takeno K, Kawaguchi M, Kakehi S, Watanabe T, et al. Effects of alcohol abstinence on glucose metabolism in Japanese men with elevated fasting glucose: A pilot study. Sci Rep. 2017;7:40277, doi: 10.1038/srep40277.

(42) Lu C, Papatheodorou SI, Danziger J, Mittleman MA. Marijuana Use and Renal Function Among US Adults. Am J Med. 2018;131(4):408-14, doi: 10.1016/j.amjmed.2017.10.051.

(43) Veronese FV, Dode RSO, Friderichs M, Thomé GG, Silva DR da, Schaefer PG, et al. Cocaine/levamisole-induced systemic vasculitis with retiform purpura and pauci-immune glomerulonephritis. Braz J Med Biol Res. 2016;49(5), doi: 10.1590/1414-431x20165244.

(44) Verna EC, Schluger A, Brown RS. Opioid epidemic and liver disease. JHEP Rep. 2019;1(3):240-55, doi: 10.1016/j.jhepr.2019.06.006.

(45) Goyal H, Rahman MR, Perisetti A, Shah N, Chhabra R. Cannabis in liver disorders: a friend or a foe? Eur J Gastroenterol Hepatol. 2018;30(11):1283-90, doi: 10.1097/MEG.0000000000001256.