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Impact of Chronic Alcohol and Opioid Dependence on Biochemical Parameters: A Retrospective Case Control Study from a Tertiary Care Treatment Center in North India

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Original Article

Abstract

Background: Assessment of biochemical parameters can help in the comprehensive management of patients with substance use disorders (SUDs). The aim of this study was to analyse the biochemical parameters of patients with alcohol and opioid dependence at an addiction treatment facility.

Methods: This retrospective study analysed the investigation reports of male patients (aged 18 to 70 years) who visited outpatient department (OPD) with primary diagnosis as opioid dependence syndrome (ODS) or alcohol dependence syndrome (ADS). The data included liver function tests (LFTs), kidney function tests (KFTs), and electrolyte tests conducted in the laboratory in a span of one year.

Findings: The study included 713 ADS, 654 ODS, and 227 controls. The ADS group showed significant elevations in mean values of bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), and gamma-glutamyl transferase (GGT) as compared to other groups. A significant decrease in albumin levels in ADS group and raised potassium levels in ODS group was observed. De Ritis ratio above threshold (AST/ALT > 2.0) alone and along with raised GGT levels was observed among 11.3% and 9.7% of patients with ADS, respectively ($P < 0.001$). Electrolyte abnormalities were present in about 20.0% of patients with ADS and ODS as compared to 8.4% among controls ($P < 0.001$).

Conclusion: LFT and electrolyte abnormalities are frequently observed in patients with alcohol and opioid dependence. De Ritis ratio along with raised GGT levels significantly denotes ADS group. These results merit attention in the course of clinical care of alcohol and opioid-dependent patients.

Keywords: Opioid; Electrolytes; Kidney; Liver

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Introduction

Alcohol and opioid abuse is listed among global burden of disease (GBD) and these substances are the most common among all the substances abused.[1] Globally, about 5.1% of adults are suffering from alcohol use disorders[2] and 0.23% of population are dependent on opioids.[1] In India, a recent national survey projected that there were about 29 million dependent users of alcohol, and 2.6 million dependent users of opioids.[3] Use of these substances often leads to physical ailments and increase in the rates of premature deaths.[4,5]

The chronic use of alcohol and opioids in a dependent manner gives rise to many physiological and biochemical changes in the functioning of important organs involved in the metabolism of these psychoactive substances.[6-8] Dependent use of alcohol and opioid is associated with derangement of enzymes and analytes pertaining to the liver function test (LFTs) and kidney function tests (KFTs), respectively. The serum transaminase ratio of 2:1 [aspartate transaminase/alanine transaminase (AST/ALT)], also known as De Ritis ratio, is suggestive of either recent alcohol exposure or advanced alcoholic liver disease and is used consistently in alcoholic population.[9,10] Chronic use of substances may also impact the kidney.[11,12] Deranged levels of serum electrolytes have been observed in patients with alcohol and opioid dependence. Chronic use of alcohol and opioid lowers the concentration of the sodium and potassium,[13,14] though contrary reports have also emerged.[15]

The biochemical changes associated with the dependent use of alcohol and opioids often reflect the alteration in homeostasis caused due to substance use, or impaired capacity of the body at self-regulation. In either case, such abnormalities, even when incidentally detected, have the potential to improve the clinical care of the patient by alerting the clinicians of the derangement. Thus, many of these tests are routinely conducted in clinical setting, with the intent of screening abnormalities. The extent and pattern of abnormalities in the screened patients can give a direction towards which issues to focus upon, and also which investigations to prioritize given a particular clinical scenario. The reporting of abnormalities in biochemical parameters has been fairly limited from the Indian addiction treatment facilities and largely focused upon LFT parameters among alcohol-dependent individuals.[16-18] Comparative analysis of alcohol and opioid-dependent individuals across multiple biochemical parameters is also lacking. Thus, this study aimed to present the pattern of LFT, KFT, and electrolyte abnormalities in patients with alcohol or opioid dependence from a treatment facility in India.

Methods

Study setting and subjects: This was a retrospective chart review carried out at a specialized addiction treatment center in North India. The center is a public-funded treatment and research facility affiliated to a medical school. It provides medically-oriented subsidized care to referred and non-referred patients. The clients comprise mainly of patients with alcohol and/or opioid dependence. The International Classification of Diseases, Tenth Revision (ICD-10) diagnostic system is generally used in the clinical services in the center. The center offers both outpatient and inpatient services and is well equipped with laboratory facilities. Blood investigations and urine drug screenings are conducted as required. The reports are made available to the treatment providers to help in the clinical care of the patients.

For the present study, biochemistry laboratory data were analysed for investigations carried out between April 2019 and March 2020. Those investigations of male patients aged 18 to 70 years were included when the patient visited the outpatient department (OPD) for the first time, the primary diagnosis noted in the requisition form was opioid dependence syndrome (ODS) or alcohol dependence syndrome (ADS), or the patient did not have any other psychiatric disorder as per records. Only men were included in the study as the women constituted less than 2% of the treatment-seeking population at the center.[19] Controls were largely staff and their family members who got their routine blood investigation done at the biochemistry laboratory in the same year. While collecting the data from controls, gender matching was done. Ethical clearance for the study was obtained from the Institutional Ethical Committee.

Biochemistry and electrolyte measurements: The routinely investigated biochemistry parameters in the laboratory were panel of tests for liver function [AST, ALT, gamma-glutamyl transferase (GGT), total bilirubin, total protein,

and albumin] and kidney function (urea, creatinine). Measurements of all the biochemistry parameters were carried out by chemistry analyser (Beckman Coulter, India Pvt Ltd). All the tests were performed as per programme by the system pack reagents based on International Federation of Clinical Chemistry (IFCC) method. Serum electrolytes like sodium and potassium were measured by electrolyte analyser (Roche, India Pvt Ltd). The measurements were carried out using respective electrodes in a buffer medium with an inbuilt reference electrode. Quality assurance of the instruments was maintained by running calibrators and quality controls with high, low, and normal levels on a daily basis. The biochemistry laboratory was a participant for external quality assessment scheme (EQA, Randox, UK) for all the measured analytes during the study period.

The laboratory data collected retrospectively were entered into Microsoft Excel sheet. Data were grouped as alcohol-dependent, opioid-dependent, or control based on primary diagnosis. The biochemical data including age were presented as descriptive statistics using mean and standard deviation (SD). One-way analysis of variance (ANOVA) or Kruskal-Wallis test was used to examine the differences among the three groups. Pairwise comparisons were done using Mann-Whitney U test, where significant group differences were present. Chi-square test was done to assess the abnormalities among each biochemical parameter or for panel of the LFT, KFT, and electrolyte across the groups. The analysis was performed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA).

Results

The laboratory data of 1594 individuals were included in the study. As per the primary diagnosis, the study included 713 alcohol-dependent patients, 654 opioid-dependent patients, and 227 control subjects. The age of the three groups is shown in table 1. It was seen that just about half of the patients in the alcohol-dependent group were in the young age group (18 to 35 years); a majority of the opioid-dependent patients and controls were in the young age group. There were significant differences in the age composition of the groups. The biochemical profile of the three groups is presented in table 2. The biochemical parameters as compared in three groups showed significant elevations in mean values of bilirubin, AST, ALT, and GGT among the alcohol-dependent group as compared to the other two groups. Albumin levels were reduced in the alcohol-dependent group as compared to opioid-dependent and control groups, while the potassium levels were higher in opioid-dependent group as compared to alcohol-dependent and control groups.

The total percentage of patients with deranged parameters among the three groups is presented in table 3. A statically significant elevation was observed in the LFT panel among patients with ADS. Among patients with alcohol dependence, more than 30% presented raised bilirubin levels, more than 50% had raised transaminase enzymes (AST and ALT), and more than 70% had elevated GGT levels. Interestingly, ODS group also showed LFT (bilirubin, AST, ALT, and GGT) elevations in 8.1%, 13.8%, 17.7%, and 20.6% of patients, respectively. About 11.3% of patients with alcohol dependence had De Ritis ratio above threshold (AST/ALT > 2.0); 9.7% of such patients had raised GGT along with De Ritis ratio above threshold. In the opioid-dependent group, the corresponding figures were 5.0% and 0.8% and in the control group, these proportions were 2.6% and 0.4%. Significant electrolyte abnormality was present in about 23.8% of patients with alcohol dependence, compared to 18.0% of opioid-dependent patients and 8.4% of controls.

The levels of serum enzymes (AST, ALT, and GGT) were displayed using histograms and Mann-Whitney test among alcohol and opioid-dependent groups (Figure 1 and Table 4).

Table 1. Age groups of the male patients (n = 1594)

Age groups (year)	ADS (n = 713) [n (%)]	ODS (n = 654) [n (%)]	Controls (n = 227) [n (%)]	Statistics
18-35	356 (49.9)	514 (78.6)	122 (53.7)	$\chi^2 = 142.300$ P < 0.001
35-55	331 (46.4)	118 (18.0)	91 (40.1)	
> 55	27 (3.8)	22 (3.4)	14 (6.2)	

ADS: Alcohol dependence syndrome; ODS: Opioid dependence syndrome

Table 2. Characteristics and laboratory parameters of the sample (n = 1594)

Parameters	ADS (n = 713)	ODS (n = 654)	Controls (n = 227)	Statistics
Bilirubin (mg/dl)	0.96 ± 0.69	0.63 ± 0.35	0.61 ± 0.23	$\chi^2 = 136.246$, $P < 0.001^*$, A > C, O
AST (U/l)	96.30 ± 95.40	44.40 ± 55.00	31.30 ± 11.00	$\chi^2 = 451.997$, $P < 0.001^*$, A > O, C
ALT (U/l)	85.90 ± 70.80	50.20 ± 67.00	34.20 ± 17.60	$\chi^2 = 319.714$, $P < 0.001^*$, A > O, C
GGT (U/l)	212.30 ± 302.50	37.90 ± 42.30	28.70 ± 15.70	$\chi^2 = 568.160$, $P < 0.001^*$, A > O, C
Total protein (g/dl)	7.28 ± 0.60	7.24 ± 0.66	7.25 ± 0.51	$\chi^2 = 5.083$, P = 0.079
Albumin (g/dl)	4.44 ± 0.54	4.46 ± 0.48	4.54 ± 0.43	$\chi^2 = 9.331$, $P = 0.009^*$, A, O < C
Urea (mg/dl)	19.50 ± 6.80	21.90 ± 6.70	22.70 ± 8.10	$\chi^2 = 64.385$, $P < 0.001^*$, A < O, C
Creatinine (mg/dl)	0.98 ± 0.18	0.99 ± 0.16	1.00 ± 0.18	F = 1.178, P = 0.308
Sodium (mmol/l)	138.30 ± 3.00	138.00 ± 2.70	138.20 ± 2.70	$\chi^2 = 4.705$, P = 0.095
Potassium (mmol/l)	4.39 ± 0.56	4.49 ± 0.48	4.38 ± 0.35	$\chi^2 = 10.495$, $P = 0.005^*$, A, C < O

Data are shown as mean ± standard deviation (SD), comparisons done using Kruskal-Wallis test or one-way analysis of variance (ANOVA), pairwise comparisons done using Mann-Whitney U test; $^*P < 0.05$

ADS: Alcohol dependence syndrome; ODS: Opioid dependence syndrome; ALT: Alanine transaminase; AST: Aspartate transaminase; GGT: Gamma-glutamyl transferase; A: Alcohol group; C: Control group; O: Opioid group

AST levels in alcohol-dependent patients varied from 5 to 1200 U/l with a majority (68.9%) measured within 50-400 U/l and very few patients (1.5%) with values going up from 400 to 1200 U/l, while in ODS, the majority (97.7%) of patients presented levels within 200 U/l. ALT levels were not much varied among the two groups with the high density of patients (97.9% and 98.5%, respectively) with levels up to 300 U/l. GGT level as considered a sensitive enzyme for alcohol intake was elevated up to 3000 U/l in alcoholic group with a majority (62.7%) measured within 50-500 U/l, while a subgroup of 10.4% had levels as high as 500-3000 U/l.

Discussion

This study provides a snapshot of the LFT, KFT, and electrolyte parameters in male patients with alcohol and opioid dependence at an addiction treatment facility.

The major finding was that the alcohol dependence was associated with derangements in bilirubin, AST, ALT, and GGT in a large proportion of the individuals. However, several LFT abnormalities were found in the opioid-dependent group as well. The De Ritis ratio coupled with raised GGT best designated the alcohol-dependent group as compared to opioid-dependent group and controls. KFT abnormalities were rare, though electrolyte abnormalities were present in about a fifth of the patients with alcohol or opioid dependence.

Abnormalities found in the alcohol-dependent group were in expected lines.[17,18,20]

Table 3. Blood values outside the normal range

Parameters	ADS (n = 713)	ODS (n = 654)	Controls (n = 227)	Statistics
Raised bilirubin	216 (30.3)	53 (8.1)	9 (4.0)	$\chi^2 = 147.227$, $P < 0.001^*$
Raised AST	401 (56.2)	90 (13.8)	11 (4.8)	$\chi^2 = 368.354$, $P < 0.001^*$
Raised ALT	388 (54.3)	116 (17.7)	23 (10.1)	$\chi^2 = 266.831$, $P < 0.001^*$
Raised GGT	518 (72.5)	135 (20.6)	24 (10.6)	$\chi^2 = 464.359$, $P < 0.001^*$
Reduced total protein	4 (0.6)	2 (0.3)	0 (0)	$\chi^2 = 0.396$, P = 0.820
Reduced albumin	37 (5.2)	13 (2.0)	5 (2.2)	$\chi^2 = 10.416$, $P = 0.005^*$
Any LFT abnormality	607 (85.0)	218 (33.3)	54 (23.8)	$\chi^2 = 470.129$, $P < 0.001^*$
AST/ALT > 2 (De Ritis ratio)	81 (11.3)	33 (5.0)	6 (2.6)	$\chi^2 = 28.525$, $P < 0.001^*$
AST/ALT > 2 and raised GGT	69 (9.7)	5 (0.8)	1 (0.4)	$\chi^2 = 71.055$, $P < 0.001^*$
Raised urea	1 (0.1)	0 (0)	2 (0.9)	$\chi^2 = 5.491$, P = 0.064
Raised creatinine	0 (0)	1 (0.2)	0 (0)	$\chi^2 = 3.154$, P = 0.207
Any KFT abnormality	1 (0.1)	1 (0.2)	2 (0.9)	$\chi^2 = 1.585$, P = 0.453
Hyponatremia	73 (10.2)	47 (7.2)	18 (7.9)	$\chi^2 = 3.707$, P = 0.157
Hypokalemia	36 (5.0)	10 (1.5)	1 (0.4)	$\chi^2 = 18.546$, $P < 0.001^*$
Hyperkalemia	76 (10.7)	68 (10.4)	0 (0)	$\chi^2 = 24.875$, $P < 0.001^*$
Any electrolyte abnormality	170 (23.8)	118 (18.0)	19 (8.4)	$\chi^2 = 26.392$, $P < 0.001^*$

Data are shown as frequency (percentage), comparisons done using Yates' chi-square; $^*P < 0.05$

ADS: Alcohol dependence syndrome; ODS: Opioid dependence syndrome; ALT: Alanine transaminase; AST: Aspartate transaminase; GGT: Gamma-glutamyl transferase; LFT: Liver function test; KFT: Kidney function test

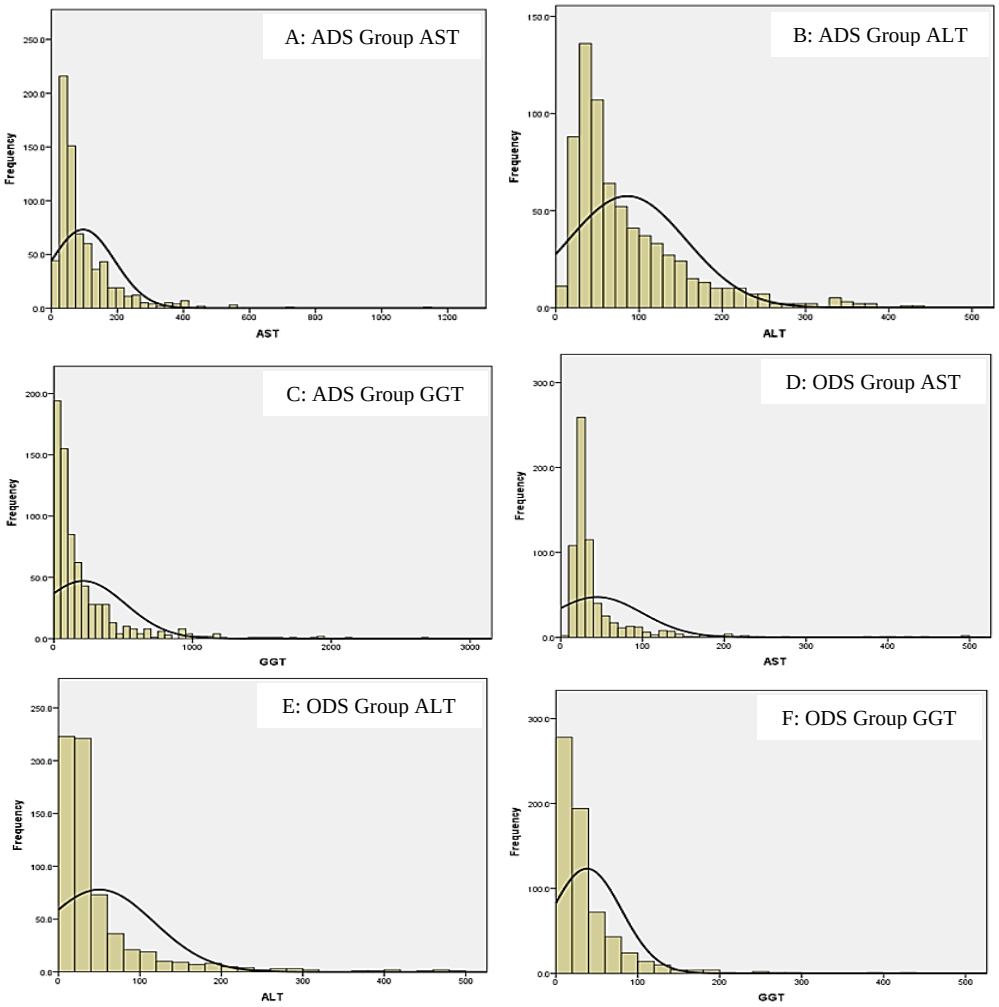

Figure 1. Histograms of aspartate transaminase (AST), alanine transaminase (ALT), and gamma-glutamyl transferase (GGT) in alcohol dependence syndrome (ADS) and opioid dependence syndrome (ODS) groups

ADS: Alcohol dependence syndrome; ALT: Alanine transaminase; AST: Aspartate transaminase; GGT: Gamma-glutamyl transferase; ODS: Opioid dependence syndrome; values of ALT, AST, and GGT are expressed in U/l

GGT, AST, and ALT were raised in more than half of the patients with alcohol dependence. This suggests that active alcohol use may lead to at least subtle dysfunctions in the liver, even though a lesser proportion may have overt features corroborated by raised bilirubin and hypoalbuminemia. Thus, asymptomatic elevations in the transaminases can suggest clinicians to take necessary interventions to prevent occurrence of potentially irreversible liver damage.

Table 4. Levels of serum enzymes in alcohol dependence syndrome (ADS) and opioid dependence syndrome (ODS) groups

Serum enzymes (U/l)	ADS (n = 713) [median (IQR)]	ODS (n = 654) [median (IQR)]	Statistics
AST	64.0 (40.0-122.0)	27.0 (21.0-41.0)	U = 95521.0, P < 0.001*
ALT	61.0 (37.0-114.0)	25.0 (17.0-51.0)	U = 116715.5, P < 0.001*
GGT	103.5 (45.0-247.0)	22.0 (16.0-42.0)	U = 74970.0, P < 0.001*

*Significant at P < 0.05

ADS: Alcohol dependence syndrome; ODS: Opioid dependence syndrome; ALT: Alanine transaminase; AST: Aspartate transaminase; GGT: Gamma-glutamyl transferase; IQR: Interquartile range

The opioid-dependent group also exhibited liver function derangements in substantial proportion of the patients. One possible explanation could be concomitant alcohol use in patients with opioid dependence, which has not escalated to the point of becoming a disorder. Previous literature suggests liver function abnormalities occurring in patients with opioid dependence who have alcohol use disorders.[21,22]

Another potential cause of transaminitis and hepatic dysfunction could be presence of viral hepatitis in this population, often contributed by sharing of injections.[23]

A previous Iranian study suggests that a minor proportion of patients on long-term methadone (about 2 years) may have abnormalities of AST and ALT.[24]

Hardly any abnormality was found in the KFTs in this population as per previous reports.[25] Electrolyte abnormalities were common in this population of alcohol and opioid-dependent individuals. Previous study by Afarinesh et al. also revealed that sodium and creatinine were found to be higher in patients with opioid dependence than controls,[26] though similar findings were not found in the present study. Many of the electrolyte abnormalities may be asymptomatic in the general or medical population.[27,28] Detection of electrolyte abnormalities may not warrant an immediate intervention, especially if the levels are not too much outside the normal range. Yet, serial monitoring may be helpful in certain cases, especially those who have a history of symptomatic electrolyte disturbances. In addition, symptomatic presentation of dyselectrolytemia can make the clinical presentation of the patient with substance use disorder (SUD) confusing (for example, it might be challenging to ascribe nausea and malaise to opioid withdrawal or hyponatremia).

There are many implications from the present study. Firstly, routine investigations of patients with alcohol use disorders may elicit abnormalities in LFT. This can be used for giving feedback during motivation enhancement, and also tracked for improvement as the patients recover from alcohol dependence. Secondly, abnormalities in LFT can be present in substantial proportion of the patients with opioid dependence as well, which could be contributed by the concomitant alcohol use or viral infection. Ascertaining alcohol use pattern and getting viral markers would help to clarify the cause and chart the next course of action. Thirdly, attention may be paid to electrolyte abnormalities and ascertaining the changes that occur with cessation of substance use and overall recovery of the patient.

The findings of the study should be considered in the context of strengths and limitations. The strengths of this study are a fairly large sample size and the presence of laboratory investigation controls. The limitations include retrospective design, limited clinical information being available apart from diagnosis and age, issues of definition in relation to 'primary diagnosis', and a single centre experience. The control group was largely referred for investigations for common medical illnesses due to such facility being available at the center, and we were unable to delineate or document medical illnesses in the control group. Besides, there could have been selection bias as not all patients might have been referred for investigations, and preferential selection of those individuals who were considered more at risk of having laboratory parameter abnormalities might have occurred. We did not include female patients in the study, and the findings may not be generalizable to women.

Conclusion

This study presents the profile of LFT, KFT, and electrolyte parameters among patients with alcohol and opioid dependence in a treatment facility. The pattern of the abnormalities can help the clinicians to chart the further course of management of the patient. Further studies can look at pattern of LFT, KFT, and electrolyte abnormalities in various combinations of SUDs, and in co-occurring of SUDs and medical disorders. Studies can also look at the temporal stability and course of different laboratory parameters, and assess whether specific parameters and their computed combinations have predictive significance.

Conflict of Interests

The Authors have no conflict of interest.

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Authors' Contribution

Conceived and designed the study protocol and were involved in data collection and sample analysis: RQ and SS; analyzed and interpreted the data: SS; drafted the article: RQ and SS; revised the article for intellectual content: RJ and SS. All the authors read and approved the final article. RQ is the guarantor of the article.

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تأثیر وابستگی مزمن به الکل و مواد مخدر بر شاخص‌های بیوشیمیایی: یک مطالعه گذشته‌نگر مورد– شاهدی از یک مرکز درمانی نوع سوم در شمال هند

رضوان قریشی[1]، سیدارت سارکار[1]، راکا جین[1]

مقاله پژوهشی

چکیده

مقدمه: ارزیابی شاخص‌های بیوشیمیایی می‌تواند به مدیریت جامع بیماران مبتلا به اختلالات مصرف مواد کمک کند. هدف از انجام پژوهش حاضر، تجزیه و تحلیل شاخص‌های بیوشیمیایی بیماران مبتلا به وابستگی به الکل و مواد مخدر در یک مرکز ترک اعتیاد بود.

روش‌ها: این مطالعه گذشته‌نگر، گزارش‌های مربوط به بیماران مرد (۱۸ تا ۷۰ ساله) را که با تشخیص اولیه به عنوان سندرم وابستگی به مواد مخدر (Opioid dependence syndrome یا ODS) یا سندرم وابستگی به الکل (Alcohol dependence syndrome یا ADS) به بخش بیماران سرپایی مراجعه کرده بودند، مورد تجزیه و تحلیل قرار داد. داده‌ها شامل آزمایش‌های عملکرد کبد (Liver function tests یا LFTs)، آزمایش‌های عملکرد کلیه (Kidney function tests یا KFTs) و آزمایش الکترولیت‌ها بود که در آزمایشگاه در یک دوره یک ساله انجام شد.

یافته‌ها: تحقیق حاضر شامل ۷۱۳ بیمار مبتلا به ADS، ۶۵۴ بیمار مبتلا به ODS و ۲۲۷ شاهد بود. گروه ADS در مقادیر میانگین بیلی‌روبین، Aspartate transaminase (AST)، Alanine transaminase (ALT) و Gamma-glutamyl transferase (GGT) در مقایسه با سایر گروه‌ها، افزایش قابل توجهی را نشان داد. کاهش قابل ملاحظه‌ای در سطح آلبومین در گروه ADS و افزایش سطح پتاسیم در گروه ODS مشاهده گردید. نسبت De Ritis بالاتر از آستانه (AST/ALT > ۲) به تنهایی و همراه با افزایش سطح GGT به ترتیب در ۱۱/۳ و ۹/۷ درصد از بیماران مبتلا به ADS مشاهده شد (P < ۰/۰۰۱). ناهنجاری‌های الکترولیت در حدود ۲۰ درصد از بیماران مبتلا به ADS و ODS در مقایسه با ۸/۴ درصد بین گروه شاهد وجود داشت.

نتیجه‌گیری: اختلالات LFT و الکترولیت‌ها اغلب در بیماران ADS و ODS مشاهده می‌شود. نسبت De Ritis همراه با افزایش سطح GGT به طور قابل توجهی نشان دهنده گروه ADS می‌باشد. این نتایج در دوره مراقبت بالینی از بیماران ADS و ODS شایسته توجه است.

واژگان کلیدی: مواد مخدر؛ الکترولیت‌ها؛ کلیه؛ کبد

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