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Original article

Evaluation of the health status outcome among inpatients treated for Amphetamine Addiction

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ABSTRACT

Amphetamine is one of the most abuser drugs in Saudi Arabia. The aim of this study was to evaluate health status outcome at baseline and after detoxification in amphetamine users through the evaluation of the body mass index, renal function tests, cardiac biomarkers, gonadal hormonal levels, and oxidative stress markers. A cross-sectional study was conducted on 90 participants. Sixty participants were hospitalized patients for treatment of addiction and 30 participants were healthy volunteers. This study was performed at a psychiatric and rehabilitation center, in Qassim region, in the Kingdom of Saudi Arabia. Participants were divided into: group I = control; group II = amphetamine users and group III = amphetamine plus cannabis users. Socio-demographic data was collected. The urinary amphetamine level, Severity Dependence Scale (SDS), body mass index (BMI), vital signs; serum levels of troponin T (TnT), immunoglobulin M (IgM), immunoglobulin G (IgG), luteinizing Hormone (LH), testosterone Hormone (TSTS), urea, creatinine, malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) were measured on admission and after detoxification. The results showed that the BMI was significantly decreased while, vital signs such as heart rate, blood pressure and respiratory rate were significantly increased in all abusers and returned to normal values after the detoxification period. The cardiac biomarker troponin T was significantly increased and reversed after detoxification. The immune system was evaluated through assessing serum levels of immunoglobulin (Ig) M and IgG. The immune system remained immunocompromised in drug users, and IgM and IgG levels did not reach the level of control group after treatment. Luteinizing and testosterone hormones were evaluated. Both hormones were increased on admission and improved after the detoxification period. Renal function showed no significant differences between drug users and the control group. In the evaluation of the antioxidant system, there was a significant increase in serum MDA, SOD, GPx, and CAT levels compared to healthy controls. After the detoxification phase, these oxidative stress biomarkers still remained elevated. The current results have shown the addiction of amphetamine and cannabis exert detrimental effects on different body organs and the exert major consequences on the health status of drug users. The present study showed that, there was no improvement in the levels of oxidative stress biomarkers, although an improvement was observed in the other parameters after the detoxification phase.

1. Introduction

Amphetamines are the most widely used unauthorized psychostimulant drugs and include amphetamine, methamphetamine (MA) and 3,4-methylenedioxy-methamphetamine (MDMA, or "ecstasy"). Amphetamines are classified as highly addictive drugs that produce stimulant effects on the central nervous system. Recently, there has been an increment in the utilization of amphetamine-type stimulants (Courtney and Ray, 2014). The reports also indicate that cannabis is the most frequently used agent followed by amphetamine, opiates, and cocaine (UNODC, 2015; El-Masry et al., 2010).

Abbreviations: SDS, Severity Dependence Scale; BMI, body mass index; TnT, vital signs, serum levels of troponin T; IgM, immunoglobulin M; IgG, immunoglobulin G; LH, luteinizing Hormone; TSTS, testosterone Hormone; MDA, urea, creatinine, malondialdehyde; SOD, superoxide dismutase; GPx, glutathione peroxidase; CAT, catalase.

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In Saudi Arabia, a retrospective study conducted by the Psychiatric Rehabilitation Center (PRC) of Buraydah, found that the most well-known drugs of abuse were amphetamine, alcohol, and cannabis. Approximately 75% of abusers are within the age group of 20–40 years. Of these, 66% were secondary school dropouts, 16.5% were elementary school children, and 9.6% were college graduates (Ibrahim et al., 2018).

In clinical practice the effects of amphetamine can be acute and prolonged. Acute effects on neurotransmitter release induce euphoria, high alertness, increased libido, and loss of appetite (Asser and Taba, 2015). High doses of amphetamine exert their effects by increasing blood pressure, hyperthermia, stroke, cardiac arrhythmia, stomach cramps, and tremors, while other acute negative psychological problems include restlessness, wakefulness, feeling aggressive, delusions, and hallucinations (Matsumoto et al., 2014; Kronstrand et al., 2018). The cardiovascular effects of amphetamine include different heart pathologies such as enlarged cardiomyopathy. Hypertension and tachycardia seem to increase with increasing doses of amphetamine due to adrenergic stimulation (Kevil et al., 2019).

Suddenly stopping high doses of amphetamines will result in physiological and mental impacts that are opposite to the acute effects of amphetamines, and include weakness, tension, irritability, depression, psychosis, insomnia, impaired thought processes, behavioral despair and even suicidal tendencies (Haj-Mirzaian et al., 2018).

The pharmacotherapy of amphetamine withdrawal is mainly symptomatic treatment. It includes benzodiazepines for anxiety, agitation and sleep disturbances, and atypical antipsychotics for amphetamine psychosis (Siefried et al., 2020). Psychosocial therapy plus pharmacotherapy is very effective in reducing Amphetamine-type stimulants (ATS) use and accompanied side effects (Tran et al., 2021).

Prolonged amphetamine abuse has been reported to cause destructive effects on the central nervous system (Yamamoto et al., 2010). Amphetamines can trigger these effects by altering the production of the cytokines interleukin (IL)-6 and tumor necrosis factor (TNF)-alpha in lipopolysaccharide (LPS)-activated microglial cells. Amphetamines alter liver function by suppressing immune reactions and by suppressing intracellular interferon alpha (IFN-α) expression in human hepatocytes (Wang et al., 2018).

Oxidative stress exerts an important role in amphetamine-induced damage of the brain, kidney, liver, and heart (Moratalla et al., 2017, Kevil et al., 2019). Thus, amphetamine-induced alteration in the function of mitochondria and dopamine oxidation that caused elevation in production of reactive oxygen species (Moratalla et al., 2017; Tung et al., 2017). Elevation of Ca2+ influx and oxide nitric synthase activity leads to formation of reactive nitrogen (Wieronska et al., 2021). Reactive oxygen and nitrogen species caused impairment and oxidation of many cellular component such as nucleic acids, lipids, and proteins (Shaerzadeh et al., 2018). The chronic toxic effects of amphetamines have been evaluated in several studies. However, there are no studies evaluating health outcomes after treatment with amphetamine addicts.

The aim of this study was to evaluate health status outcomes among inpatients Treated for Amphetamine Addiction through the evaluation of the BMI, renal function tests, cardiac biomarkers, gonadal hormonal levels, and oxidative stress biomarker values.

2. Subjects and methods

2.1. Subjects

This was a cross sectional study conducted at the Psychiatric and Rehabilitation Centre (Al Amal Hospital for Mental Health), Qassim region, Kingdom of Saudi Arabia, and included 90 participants. All participants were free of any underlying medical condition and had similar dietary habits. The participants were divided equally into three groups: Group I: Control group (n = 30), participants were healthy individuals without clinical evidence and negative urine screen for drugs of abuse. group; Group II: amphetamine user group (n = 30) and Group III: combined drug users (amphetamine plus cannabis) (n = 30). Patients were interviewed by experienced psychiatrists and were evaluated according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria. Patients were screened daily for the presence withdrawal syndrome. The control group participants were frequency-matched to the exposed group in terms of lifestyle and age. For each participant, the general medical history, smoking status, and history of substance use were obtained. The following inclusion and exclusion criteria were then applied:

Inclusion criteria: Patients who were treated under same regimen and first attempt for treatment. Moreover, anti-oxidant were not included in treatment of our patients.

Exclusion criteria: Individuals with a history of medical diseases such as liver, renal, hematological, and immune diseases, or patients received any medication that might affect the biochemical parameters and non-cooperativeness patients.

2.2. Ethics statement

Study approval was obtained from the college, university ethics committee and The Research Ethics Committee at the Ministry of Health, Saudi Arabia. In addition, consent was obtained from each participant.

2.3. Serum collection and storage

Blood samples were collected under complete aseptic conditions by clean venipuncture using sterile disposable syringes. Approximately 10 mL of blood was withdrawn from each drug user as well as from controls. Blood was delivered into clean dry test tubes and was allowed to clot at room temperature. Whole blood was centrifuged at 1600 rpm for 5 min. and the serum was aliquoted into 1.7 mL Eppendorf tubes. Serum samples were stored in tightly closed vials at −80 °C until use. The samples were collected at admission and after the detoxification period (21 days of treatment).

2.4. Urine collection and storage

A 25 mL volume of urine was collected in a plastic container at admission under quality control and safety procedures, and was frozen at −20 °C until analysis. The samples were collected on the first day of admission (day 1) and at the end of the detoxification period (21 days of treatment).

2.5. Severity dependence scale

The Severity Dependence Scale (SDS) is a 5-point questionnaire that provides an overview of the severity of the substance use disorder dependency. The 5 items on the scale are measured on a 4-point scale of 0–3. The overall score is obtained by adding the 5-point scores (Gossop et al., 1995).

2.6. Determination of urinary amphetamine level

The urine specimens were collected immediately after hospital admission at emergency department then it was examined for amphetamine abuse by emerging the multidrug screen kit in the urine, then waiting about 5 min. If the result positive, we send a

urine sample for laboratory to quantitative measurement of the level of amphetamine in the urine. After detoxification phase, the second sample drawn from addicts then send it again to laboratory for checking. Urinary amphetamine levels were measured using Abbott multigent amphetamine/methamphetamine assay kit with catalog number (REF 3L37-20) (Thermo scientific, CA, USA). The assay uses monoclonal antibodies that detect amphetamine and/or methamphetamine in urine. The assay was centered on the competition for a fixed number of unique antibody binding sites between an enzyme labelled drug and the drug from the urine. In the absence of the drug, the antibody binds to the drug labelled with glucose-6-phosphate dehydrogenase (G6PDH) and inhibits enzyme activity. The capacity of the G6PDH enzyme to convert nicotinamide adenine dinucleotide (NAD) to NADH was measured spectrophotometrically at 416 nm (Armbruster et al., 1993). All samples were measured in triplicate.

2.7. Determination of serum troponin T

Serum levels of the cardiac troponin T hormone (TnT) were measured using the Roche Cobas e 411 analyzer for quantitative electrochemiluminescence immunoassays. The kits used for Troponin T were obtained from Roche Diagnostics (Basel, Switzerland) (catalog number 05092744 190). Briefly, 50 µl of the sample, biotinylated monoclonal cardiovascular troponin and a monoclonal cardiac troponin T specific antibody cardiac antibody marked with ruthenium complex A were incubated to form a spring-specific sandwich complex. The complex was bound to the solid phase by association of biotin and streptavidin following the addition of strappavidin-related microparticles. The reaction mixture was last vacuumed in a measuring cell in which the microparticles are magnetically captured on the electrode surface. The results were reported according to the selected option in the system. All samples were measured in triplicate.

2.8. Determination of serum immunoglobulin levels

Commercially available MININEPHTM nephelometry kits (Binding site, Birmingham, UK) were used to determine IgG and IgM levels. Immediately prior to analysis, the serum samples and reagents were brought to room temperature and 1:10 dilutions (40 µl of sample in 400 µl of diluent) were prepared. A cuvette was positioned in the cuvette holder and in this were mixed the buffer (400 µl) and anti-immunoglobulin (40 µl) with 10 µl of sample for the IgG assay or 40 µl of sample for the IgM assays. All samples were measured in triplicate.

2.9. Determination of serum testosterone

Serum testosterone (TSTS) levels were measured using Siemens ADVIA Centaur XP (Siemens Healthcare Diagnostics, Erlangen, Germany). In brief, TSTS in the sample competes for binding against antimonoclonal antibody with acridinium ester named hapten in the Lites Reagent. The trial uses a testosterone releasing agent from the samples, ADVIA Centaur, to release tied testosterone from the endogenous binding protein. Reagents were first used in a 10.0 mL/reagent package of Acridinium ester-labelled Hapten (36 µg/mL) in the buffered saline with preservatives in ADVIA Centaur TSTII ReadyPack® primary reagent (Lite Reagent). Second, the primary reagent package (Solid Phase reagent) of ADVIA Centaur TSTII was made of 17.0 mL/reagent packaging streptavidin-coated latex particles (0, 33 g/L). The release agent included a ready pack of ancillary reagent ADVIA Centaur testosterone II which had 10.0 mL/Reagent Steroid Releasing Agent (0.4 µg/mL) and ancillary anti-testosterone (27 µg/L) bio-tinylated sheep in buffered saline and preservatives. The machine conducted test procedures automatically as follows: dispensing the sample (20 µl) and the release agent (90 µl) into a cuvette and were incubated at 37 °C for 25 min; discharging 50 µl of Lite Reagent and 150 µl of Solid Phase were incubated for 75 min at 37 °C, detaching, aspiring, and washing the cuvettes. Wash and final stage were used to dump the chemiluminescent reaction with 300 µl of each acid reagent and base reagent. All samples were measured in triplicate.

2.10. Determination of serum luteinizing hormone

Serum luteinizing hormone (LH) levels were measured using Siemens ADVIA Centaur XP (Siemens Healthcare Diagnostics, Erlangen, Germany). The ADVIA Centaur LH test is a two-site immunoassay sandwich using direct chemiluminometric technology, which uses a consistent number of two antibodies that are unique for the intact LH molecule beta. An anti-LH monoclonal antibody with acridinium ester is the first antibody in the lite reagent. The second antibody, in the solid phase, which is covalently bound to paramagnetic particles, is a monoclonal mouse anti-LH antibody. Second, the primary reagent kit (Lite Reagent), which was labelled with Acridinum Ester (<0.1%) buffers with sodium azide and preservatives, was used as ADVIA Centaur LH Ready Pack, a single anti-LH (~0.17 µg/mL) mono-clonal mouse package. The second reagent was the sodium azide (0.1 percent) and preservative, 24.0 mL/reagent packaging, monoclonal mouse anti-LH antibody (~0.05 mg/mL) ADVIA Centaur LH Ready reagent package. The diluents were used as an auxiliary reagent (multi-diluent) package of ADVIA Centaur, 25.0 mL/reagent packaging for equine serum with sodium azide (0.1%) and preservatives. The machine was conducted test procedures automatically as follows: spending 50 µl of the sample in cuvette, dispensing 100 µl of the Lite Reagent and was incubated at 37 °C for 50 min; dispensing the Solid Phase with 400 µl and incubating it for 2.5 min at 37 °C, separating the aspirate and washing the reagent and cuvettes with water and dispensing with Acid Reagent and Base Reagent to cause the chemiluminescent reaction. All samples were measured in triplicate.

2.11. Determination of kidney function tests

The serum concentrations of urea were determined using a commercially available kit supplied by Diamond (Saudi Arabia) following the approach described by Patton and Crouch (1977). The concentration of creatinine (Cr) in the serum was determined according to the protocol described by Bowers and Wong (1980) with a commercially available kit (Diamond, Saudi Arabia).

2.12. Determination of biomarkers of oxidative stress

2.12.1. Determination of serum malondialdehyde levels

Serum malondialdehyde levels were measured quantitatively using an ELISA kit obtained from Myobiosource Company, United States of America (catalog number: MBS263626). The preparation of for the experiment were started by got out the Elisa Kit out of refrigerator for 20 min in advance and take test when it balances at room temperature. Then, dilute the concentrated washing solution with double distilled water (1:25). 100 µl of standards or samples were added to their corresponding wells. The plate was sealed with the adhesive tape strip and incubated at 37 °C for 90 min. ELISA plate was washed two times and biotinylated Antibody was added to each well (100 µl per well). The plate was sealed with the adhesive tape strip and incubated at 37 °C for 60 min. ELISA plate was washed three times. 100 µl of Enzyme Conjugate was prepared and added to each well. The plate was sealed with the adhesive tape strip and incubated at 37 °C for 30 min. 10. ELISA plate was washed five times. 100 µl of the prepared Color Reagent

was added to each well and incubated at 37 °C in the dark. 100 µl of Color Reagent C was added to each well Finally the mixture was mixed well. Then, we read optical density at 450 nm within 10 min. All samples were measured in triplicate.

2.12.2. Determination of serum superoxide dismutase activity

The serum superoxide dismutase activity was measured quantitatively using an ELISA kit obtained from Myobiosource Company, United States of America (catalog number: MBS262339). The preparation of for the experiment were started by got out the Elisa Kit out of refrigerator for 20 min in advance and take test when it balances at room temperature. Then, 100 µl of samples or standards were added to corresponding wells. The reaction wells were sealed with adhesive tapes and incubated at 37 °C for 90 min. Elisa plate was washed two times and 100 µl of the biotinylated human SOD antibody liquid was added to each well. The reaction wells were sealed with adhesive tapes and incubated at 37 °C for 60 min. Elisa plate was washed three times and 100 µl of enzyme-conjugate liquid was added to each well. The reaction wells were sealed with adhesive tapes and incubated at 37 °C for 30 min. Elisa plate was washed five times and 100 µl of Colour Reagent liquid was added to each well and incubated away from light at 37 °C. Finally, 100 µl Colour Reagent C was added to each well and mixed well. Then, we read optical density at 450 nm within 10 min. All samples were measured in triplicate.

2.12.3. Determination of serum glutathione peroxidase activity

The serum glutathione peroxidase activity was measured quantitatively using an ELISA kit obtained from the Myobiosource Company from the United States of America (USA) (catalogue number: MBS167041). The preparation of for the experiment were started by got out the Elisa Kit out of refrigerator for 20 min in advance and take test when it balances at room temperature. Then, 50 µl of the standards was added to corresponding wells and 40 µl of the sample was added to sample wells. 10 µl of anti-GPX antibody was added to sample wells, then 50 µl streptavidin-HRP was added to the sample wells and standard wells. Then, the mixtures were mixed well. The plate was sealed and incubated for 60 min at 37 °C. The plate was washed five times with wash buffer. The wells were washed with 0.35 mL of the wash buffer for 1 min each time. 50 µl of the substrate solution A was added and then add 50 µl substrate solution B to each well. The plate was incubated in the dark for 10 min at 37 °C. 50 µl of the Stop Solution was added to each well. The optical density was determined immediately at 450 nm within 10 min. All samples were measured in triplicate.

2.12.4. Determination of serum catalase activity

The serum Catalase Activity ELISA kit was used to quantitatively measure the serum levels of human CAT. The kit was obtained from MyBioSource Co. (USA; catalog number: MBS2600178). The preparation of for the experiment were started by got out the Elisa Kit out of refrigerator for 20 min in advance and take test when it balances at room temperature. Then, 100 µl of samples or standards were added to corresponding wells. The reaction wells were sealed with adhesive tapes and incubated at 37 °C for 90 min. Elisa plate was washed two times and 100 µl of the prepared Enzyme Conjugate was added to each well. The reaction wells were sealed with adhesive tapes and incubated at 37 °C for 60 min. 100 µl of the Color Reagent C was added to wells. The optical density was determined immediately at 450 nm within 10 min. All samples were measured in triplicate.

2.13. Statistical analysis

Data were collected, tabulated, and statistically analyzed by one-way analysis of variance (ANOVA) for significant of differences in the compared to non-drug user controls. Results were expressed as means ± SD and were considered statistically significant if the *P*-value < 0.05. Pearson's correlation coefficients were used to determine the relationships between the duration of addiction, amphetamine levels, cardiac, renal, and immunological parameters, and oxidative stress biomarkers. GraphPad prism software Version 8.4.3(GraphPad software, San Diego, CA) package was used for all statistical analyses.

3. Results

The present study reported that, nine patients from group II and III did not continue their treatment and were excluded from the study groups.

3.1. Socio-demographic characteristics

The ages of the participants ranged from 20 to 58 years, with mean ages of 32.9 ± 8.52, 34.23 ± 7.95 and 29.77 ± 6.92 years in groups I, II, and III, respectively. There were no significant changes between the three studied groups with regard to age range (P > 0.05). Most of the studied participants were from urban areas: group I, II and III 63.34, 60.00, and 63.34%, respectively. Regarding the distribution of the studied participants according to their marital status, the present study indicated that, in groups I and II more than half of the patients were married 63.34 and 53.34%, respectively. In group III more than half of patients were single 76.67%. In the present study, most of participants were living with their families 76.67%, 66.67%, and 63.34% in groups I, II, and III, respectively. Regarding the distribution of the participants according to their highest educational level, the present study revealed that the highest percentage of participants were high secondary school graduates (66.67%, 60.00% and 76.67% in groups I, II, and III, respectively). The majority of participants were employed 60%, 46.66%, and 60% in groups I, II, and III, respectively. The present study showed that all patients were current cigarette smokers and caffeine users (Table 1).

3.2. Duration of drug use

As demonstrated in Table 2, the duration of amphetamine uses in the studied patients ranged from 2 to 22 years, with a mean duration of 8.13 ± 4.93 years in group II. While, the duration of amphetamine plus cannabis intake in the studied patients ranged from 2 to 17 years, with a mean duration 6.06 ± 3.56 years in group II. Regarding the duration of intake, the study showed that there were no significant changes between the two groups of drug users (groups II and III, P > 0.05).

3.3. Motivation for use of drug substances

The motivations declared by participants for practicing drug use, the influence of friends represented the most common cause for starting and continuing intake: 40% and 60% in groups II and III, respectively. In addition, life style stress, frustration, and relationship difficulties were important reasons for substance use disorder; these factors represented 23.33%, 16.66%, and 16.66% in group II, while, they represented 16.66%, 13.34%, and 6.67% in group III (Table 3).

3.4. Amphetamine level and severity dependence scale

Amphetamine levels were 1519.71 ± 683.16 and 1471.25 ± 727.82 (ng/mL) for groups II and III at admission. The severity dependence scale values were 10.86 ± 2.47 and 10.06 ± 2.30 for groups

Table 1
Distribution of the control and addict groups (n = 90) according to their ages, Residence, Marital status, Social status, Educational levels, Occupational status and Special habits.

Items		Group I (n = 30)	Group II (n = 30)	Group III (n = 30)
Age (years) Mean ± SD		32.9 ± 8.52	34.23 ± 7.95	29.77 ± 6.92
Residence (%)	**Urban**	63.34	60	63.34
	Rural	36.66	40	36.66
Marital status (%)	**Single**	36.66	36.66	76.67
	Married	63.34	53.34	10
	Divorced	0	10	13.33
Social status (%)	**Living with family**	76.67	66.67	63.34
	Living alone	0	6.67	0
	Living with friends	23.33	26.66	36.66
Educational levels (%)	**Non-educated**	0	3.33	0
	Primary school	0	20	6.67
	Intermediate school	0	13.34	10
	High Secondary school	66.67	60	76.67
	High education	33.33	3.33	0
Occupational status (%)	**Student**	33.33	13.34	13.34
	Job	60	46.66	60
	Jobless	6.67	40	26.66
Special habits (%)	**Smoker**	100	100	100
	Caffeine user	100	100	100

Group I – Control group; Group II – Amphetamine group; Group III- Amphetamine plus Cannabis group.
P-value has been calculated using One-Way ANOVA test.
* Significant at p < 0.05 level.

Table 2
Distribution of the addict groups (n = 90) according to the duration of Amphetamine or Amphetamine plus cannabis intake (years).

Duration of intake (years)	Group II (n = 30)			Group III (n = 30)		
	No.	%	Mean ± SD	No.	%	Mean ± SD
2 – <3	1	3.33	8.13 ± 4.93	3	10	6.06 ± 3.56
3 – <4	5	16.66		3	10	
4 – <5	4	13.34		5	16.66	
≥5	20	66.67		19	63.34	

Group II – Amphetamine group; Group III- Amphetamine plus Cannabis group.
Fischer Exact test.
* Significant at p < 0.05 level.

II and III at admission. There were no significant changes in mean amphetamine levels or in the SDS values comparing group II with group III (Table 4).

3.5. Body mass index

As shown in Table 5, there was a significant decrease in the mean BMI values at baseline and after the detoxification phase in groups II and III compared with the control group) P > 0.05). The mean BMI values after the detoxification phase in groups II and III demonstrated no significant changes in BMI compared with the corresponding baseline values. BMI showed improvement over the three weeks of detoxification.

Table 3
Distribution of the control and addict groups (n = 90) according to their motives for substance intake.

Motives for substance intake	Group II (n = 30)		Group III (n = 30)	
	No.	%	No.	%
Life style stress	7	23.33	5	16.66
Influence of friends	12	40	18	60
Frustration	5	16.66	4	13.34
Relationship difficulties	5	16.66	2	6.67
Others	1	3.33	1	3.33

Group II – Amphetamine group; Group III- Amphetamine plus Cannabis group.

Table 4
Amphetamine level and severity dependence scale (SDS) for addict groups (n = 60) at admission.

Items	Group II (n = 30)	Group III (n = 30)
Amphetamine level (ng/mL)	1519.71 ± 683.16	1471.25 ± 727.82
SDS	10.86 ± 2.47	10.06 ± 2.30

Group II – Amphetamine group; Group III – Amphetamine + Cannabis group; SDS – Severity Dependence Scale.
P-value has been calculated using One-way ANOVA test.
*Significant at P < 0.05 level.

3.6. Vital signs

There was no significant change in the mean temperature values between baseline and after detoxification in groups II and III compared with the control group. In addition, the mean temperature values after the detoxification phase in groups II and III demonstrated no significant changes compared with the corresponding baseline values (Table 5). As shown in Table 5, there was a significant increase in mean heart rate values at baseline and significant decrease after the detoxification phase in groups II and III compared with control group (P < 0.05). The mean heart rate after the detoxification phase demonstrated significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05). There was a significant increase in the mean SBP values at baseline (P < 0.05) and no significant changes were observed after the detoxification phase in groups II and III compared with controls. The mean SBP values after the detoxifica-

tion phase demonstrated a significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05) (Table 5). There was a significant increase in the mean DBP values at baseline and after the detoxification phase in groups II and III compared with the control group (P < 0.05). The mean DBP values after the detoxification phase demonstrated significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05) (Table 5). There was a significant increase in the mean RR values at baseline and after the detoxification phase in groups II and III compared with control group (P < 0.05). The mean DBP values after the detoxification phase demonstrated a significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05) (Table 5). All the markers of vital signs (temperature, heart rate, SBP, DBP, RR) showed improvement over the three weeks of detoxification.

3.7. Serum troponin T level

As shown in Fig. 1, there was a significant increase in the mean TnT values at baseline in groups II and III compared with the control group (P < 0.05). The mean TnT values after the detoxification phase demonstrated a significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05). The cardiac markers (troponin T) showed improvement over the three weeks of detoxification.

3.8. Serum immunoglobulin M an G levels

As shown in Fig. 2, there was a significant decrease in the mean IgM and IgG values at baseline and after the detoxification phase in groups II and III compared with the control group (P < 0.05). The mean IgM values after the detoxification phase demonstrated significant increase in groups II and III compared with the corresponding baseline values (P < 0.05). The mean IgG values after the detoxification phase demonstrated significant decrease in group II and increase in group III with the corresponding baseline values (P < 0.05). The markers of inflammation (IgM) showed improvement in groups II and III over the three weeks of detoxification. While, IgG showed improvement in groups II over the three weeks of detoxification.

3.9. Serum luteinizing hormone and testosterone levels

There was a significant increase in the mean LH and TSTS hormone values at baseline and after the detoxification phase in the groups II and III compared with the control group (P < 0.05). The mean LH and TSTS hormone values after the detoxification phase demonstrated significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05) (Fig. 3). The

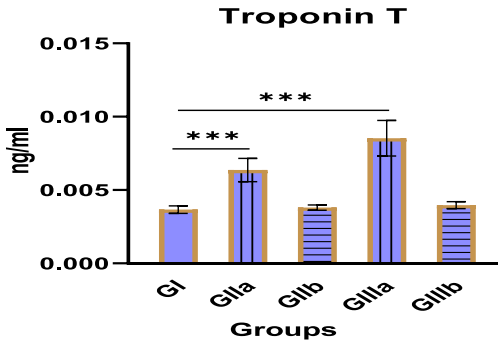

Fig. 1. Serum level of Troponin T on admission and after detoxification for control and addict groups. GI – Control group; GIIa – Amphetamine group at admission; GIIb – Amphetamine group after detoxification phase; GIIIa – Amphetamine Plus Cannabis group at admission; GIIIb – Amphetamine Plus Cannabis group after detoxification phase. N = 90.

gonadal hormones (LH and TSTS) showed improvement over the three weeks of detoxification.

3.10. Serum urea and creatinine levels

As shown in Table 6, there was no significant change in the mean urea and creatinine values at baseline and after the detoxification phase in groups II and III compared with the control group. The mean urea and creatinine values after the detoxification phase demonstrated no significant changes in groups II and III compared with the corresponding baseline values. The markers of the kidney showed no change at the baseline or over the three weeks of detoxification.

3.11. Serum oxidative stress biomarker levels

There was a significant increase in the mean MDA, SOD, GPx and values at baseline and after the detoxification phase in the groups II and III compared with the control group (P < 0.05). The mean MDA, SOD, GPx and CAT values after the detoxification phase demonstrated significant decrease in groups II and III compared with the corresponding baseline values (P < 0.05). (Fig. 4). All the markers of oxidative stress (MDA, SOD, GPx, CAT) showed improvement over the three weeks of detoxification'

3.12. Correlations of the studied parameters

3.12.1. Body mass index

There were no significant correlations at baseline in groups II and III between BMI and SDS score (Table 7**)**. Although, there were

Table 5
Body mass index and vital signs for the control and addict groups (n = 90) at admission (AA) and after the detoxification phase (AD).

Items	Group I (n = 30)	Group II (n = 30)		Group III (n = 30)	
		AA	AD	AA	AD
BMI (kg/m²)	28.63 ± 1.85	24.91 ± 2.90[a]	25.44 ± 2.87[a]	24.36 ± 2.90[a]	24.72 ± 2.87[a]
Temp. (°C)	36.93 ± 0.04	37.02 ± 0.04	36.96 ± 0.04	36.95 ± 0.04	37.01 ± 0.04
HR (bpm)	82.30 ± 2.62	94.37 ± 2.62[a]	80.07 ± 1.51[ab]	98.70 ± 2.62[a]	78.90 ± 1.51[ab]
SBP (mmHg)	121.00 ± 3.72	139.50 ± 3.72[a]	120.10 ± 1.57[b]	139.30 ± 3.72[a]	121.50 ± 1.57[b]
DBP (mmHg)	77.90 ± 1.89	86.53 ± 1.89[a]	79.20 ± 1.04[ab]	86.97 ± 1.89[a]	80.83 ± 1.04[ab]
RR (bpm)	17.80 ± 0.28	20.27 ± 0.24[a]	18.87 ± 0.28[ab]	20.43 ± 0.28[a]	19.17 ± 0.24[ab]

Group I – Control group; Group II – Amphetamine group; Group III- Amphetamine plus Cannabis group; SDS- Severity Dependence Scale; Temp- Temperature; BMI- Body Mass Index; HR- Heart Rate; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; RR- Respiratory Rate; AA – At Admission; AD- After detoxification. Values expressed as Mean ± SD.
Significant at p < 0.05 level.
[a] Significant compared with control group.
[b] Significant compared at admission and after detoxification phase in the same group.

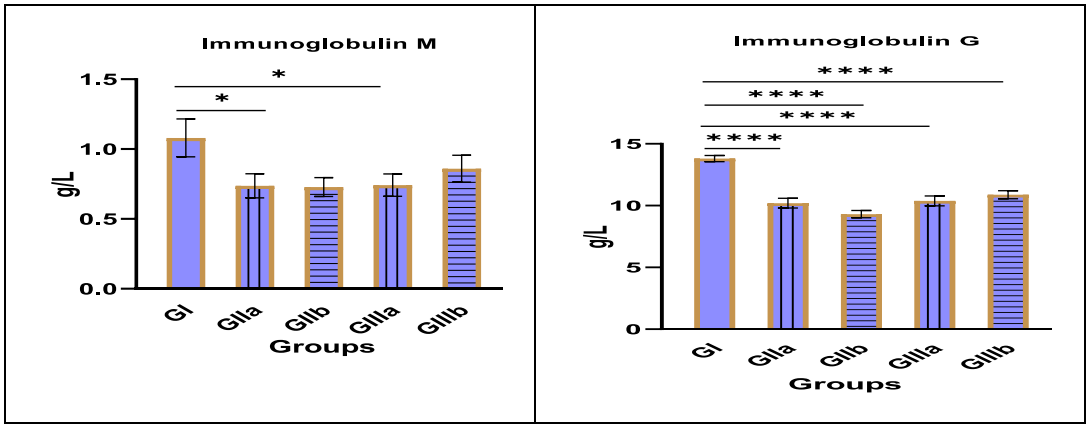

Fig. 2. Serum level of immunoglobulin M and G on admission and after detoxification for control and addict groups. GI – Control group; GIIa – Amphetamine group at admission; GIIb – Amphetamine group after detoxification phase; GIIIa – Amphetamine Plus Cannabis group at admission; GIIIb – Amphetamine Plus Cannabis group after detoxification phase. N = 90.

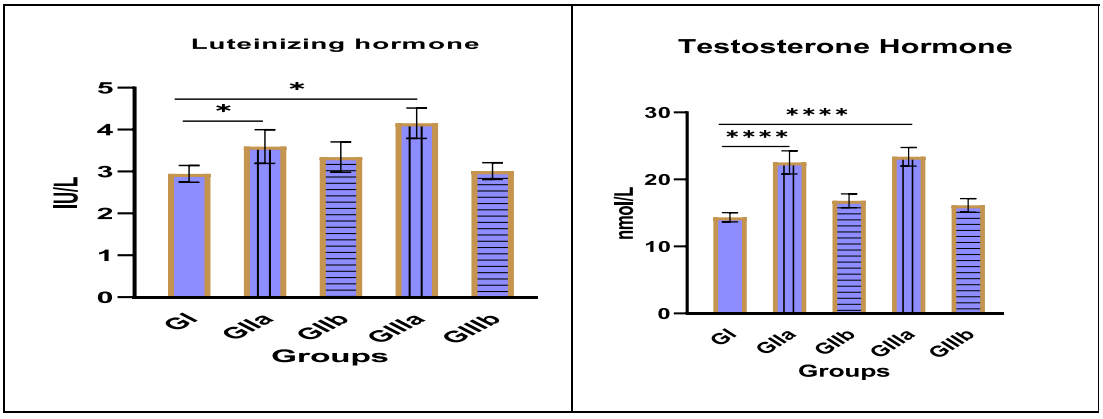

Fig. 3. Serum level of Luteinizing and testosterone hormones on admission and after detoxification for control and addict groups. GI – Control group; GIIa – Amphetamine group at admission; GIIb – Amphetamine group after detoxification phase; GIIIa – Amphetamine Plus Cannabis group at admission; GIIIb – Amphetamine + Cannabis group after detoxification phase. N = 90.

no significant correlations at baseline between groups II and amphetamine level, a positive significant correlation was observed in group III for BMI and amphetamine level. In groups II and III, there was positive significant correlation between BMI and the age of participants. BMI showed a positive significant correlation in group II and no significant correlation in group III with the duration of addiction.

3.12.2. Vital signs

Body temperature was positively significantly correlated in group II and negatively significantly correlated in group III with the SDS at baseline (Table 7). There were no significant correlations at baseline in group II between body temperature, amphetamine level, age of participants, or duration of addiction. In group III, there was a positive significant correlation between body temperature, amphetamine level, age of participants, and duration of addiction at baseline. HR was not significantly correlated with SDS or amphetamine levels in groups II and III (Table 7). In addition, there were no significant correlations between HR, age of participants, or the duration of addiction at baseline. In contrast, HR showed a positive significant correlation with the age of participants and duration of addiction in group III at baseline. SBP showed a positive significant correlation with age of participants in groups II and III at baseline (Table 7). Conversely, SBP showed no signifi-

Table 6
Kidney function tests for the control and addict groups (n = 90) at admission (AA) and after the detoxification phase (AD).

Items	Group I (n = 30)	Group II (n = 30)		Group III (n = 30)	
		AA	AD	AA	AD
Urea (mmol/L)	4.713 ± 1.32	4.567 ± 1.27	4.417 ± 0.73	4.163 ± 0.78	4.183 ± 0.67
Creatinine (μmol/L)	75.60 ± 12.9	78.78 ± 11.4	74.65 ± 10.2	78.71 ± 11.7	78.60 ± 10.7

Group I – Control group; Group II – Amphetamine group; Group III – Amphetamine plus Cannabis group; AA – At Admission; AD – After detoxification. Values expressed as Mean ± SD.
[a] Significant compared with control group.
[b] Significant compared at admission and after detoxification phase in the same group.
Significant at $p < 0.05$ level.
P-value has been calculated using One-Way ANOVA test.

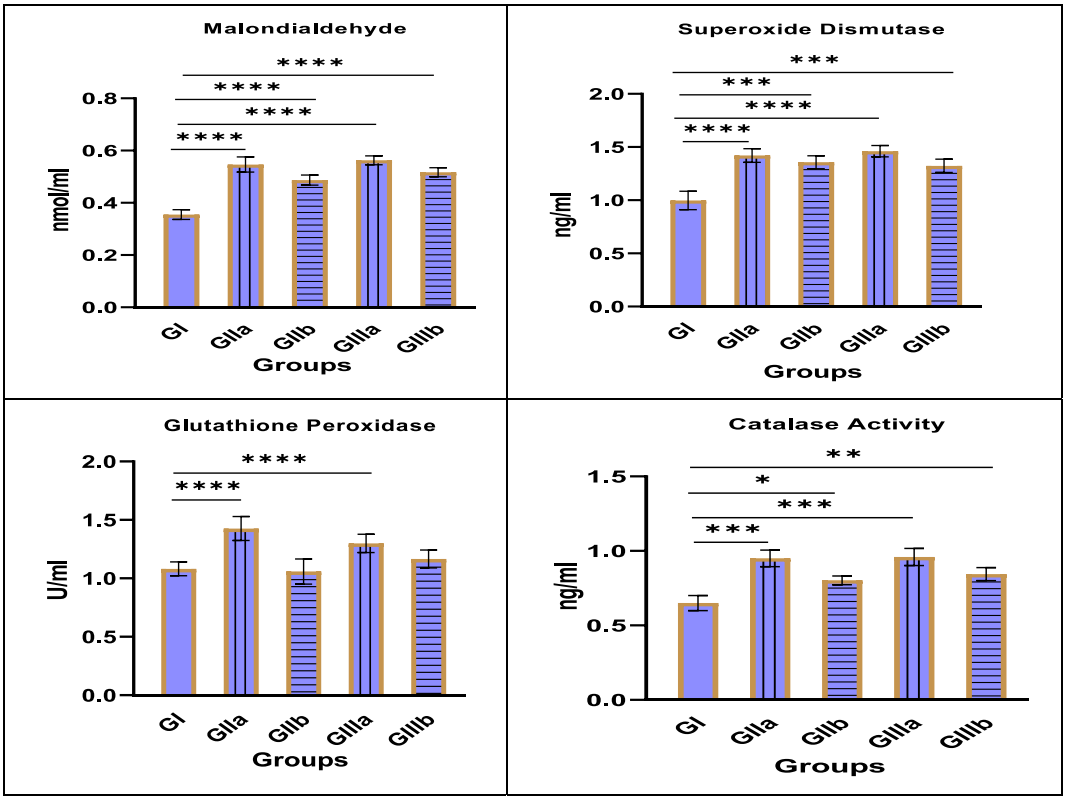

Fig. 4. Serum level of malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) activities on admission and after detoxification for control and addict groups. GI – Control group; GIIa – Amphetamine group at admission; GIIb – Amphetamine group after detoxification phase; GIIIa – Amphetamine + Cannabis group at admission; GIIIb – Amphetamine + Cannabis group after detoxification phase. N = 90.

cant correlations with the SDS, amphetamine level, or duration of addiction in both groups at baseline. DBP showed no significant correlation with SDS in groups II and III at baseline (Table 7). Conversely, DBP showed a positive significant correlation in group II and no significant correlation in group III with amphetamine levels or duration of addiction at baseline. In groups II and III, there was positive significant correlation between DBP and the age of participants at baseline. RR showed no significant correlation with SDS in

Table 7
Pearson correlation coefficients between Severity Dependence Scale (SDS), Amphetamine level, Age and duration of Addiction, Body Mass Index (BMI) and Vital Signs in the addicts at baseline.

Items	SDS		Amphetamine level		Age		Duration of addiction	
	Group II	Group III	Group II	Group III	Group II	Group III	Group II	Group III
BMI (kg/m$^{2)}$	−0.12	−0.14	0.6577	0.5232	−0.09028			
	−0.06	0.65***	0.29**	0.52**	0.41**	−0.09		
Temp. (°C)	0.20*	−0.27*	0.2045	0.3616	0.3216			
	0.02	0.20*	0.07	0.36**	0.18	0.32**		
HR (bpm)	−0.10	−0.03	0.14	0.09	0.10	0.41**	0.08	0.25*
SBP (mmHg)	−0.04	0.005	0.11	0.04	0.219*	0.46**	0.15	0.19
DBP (mmHg)	−0.09	0.005	0.22*	0.04	0.27 *	0.46**	0.28*	0.19
RR (bpm)	−0.19	−0.14	0.29*	0.28*	−0.02	0.42**	−0.03	0.30**
TnT (ng/ml)	0.003	0.06	0.26 *	0.15	−0.01	0.07	0.01	0.04
IgM (g/L)	−0.05	−0.07	0.17	0.29*	0.001	0.13	−0.08	0.01
IgG (g/L)	−0.20*	−0.24*	0.002	−0.04	0.12	0.19	−0.003	0.10
LH (IU/L)	0.034	0.30**	0.07	−0.18	−0.05	−0.004	−0.03	−0.09
TSTS (nmol/L)	−0.17	−0.32**	−0.18	−0.28*	−0.16	−0.39**	−0.13	−0.21*
Urea (mmol/L)	0.28*	0.25*	0.18	0.12	0.32 **	0.33**	0.29 *	0.37**
Creatinine (µmol/L)	0.01	0.002	0.16	0.05	0.31 **	0.63**	0.11	0.47**
SOD (ng/ml)	0.25*	0.21*	−0.062	0.29*	−0.12	−0.15	−0.24*	−0.19
MDA (nmol/ml)	0.10	0.19	0.12	0.38**	−0.06	−0.20*	0.02	−0.21*
GPx (U/ml)	−0.02	0.18	0.51**	0.49**	−0.013	0.23*	0.09	0.30**
CAT (ng/ml)	0.02	−0.01	0.20*	0.05	0.008	−0.02	−0.09	−0.07

Group II – Amphetamine group; Group III – Amphetamine plus Cannabis group; SDS – Severity Dependence Scale; Temp – Temperature; BMI – Body Mass Index; HR – Heart Rate; SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; RR – Respiratory Rate; TnT – troponin T; IgM – immunoglobulin M; IgG – immunoglobulin G; LH – luteinizing hormone; TSTS – testosterone; SOD – superoxide dismutase; MDA – malondialdehyde; GPx – glutathione peroxidase and CAT – catalase.
* Correlation was statistically significant at 0.05 level (2-tailed).
** Correlation was statistically significant at 0.01 level (2-tailed).

groups II and III at baseline (Table 7). RR showed a positive significant correlation in groups II and III with amphetamine level at baseline. In addition, RR showed a positive significant correlation in group III and no significant correlation in group II with the age of participants or duration of addiction.

3.12.3. Serum troponin T level

Serum TnT levels showed a positive significant correlation in group II and no significant correlation in group III with the amphetamine level at baseline (Table 7). Conversely, TnT levels showed no significant correlations with the SDS, age of participants, or duration of addiction in both groups at baseline.

3.12.4. Serum immunoglobulin M and G level

IgM levels showed a positive significant correlation in group III and no significant correlation in group II with the amphetamine level at baseline (Table 7). Conversely, IgM level showed no significant correlation with the SDS, age of participants, or duration of addiction in both groups at baseline. IgG levels showed a negative significant correlation in groups II and III with the SDS at baseline (Table 7). Conversely, IgG levels showed no significant correlation with the amphetamine level, age of participants, or duration of addiction in both groups at baseline.

3.13. Serum luteinizing hormone and testosterone levels

Serum LH levels showed no significant correlation with the SDS in group II but was positively and significantly correlated in group III at baseline. Conversely, LH levels showed no significant correlation with the amphetamine level, age of participants, or duration of addiction in both groups at baseline. TSTS level showed no significant correlation in group II and negative significant correlation in group III with the SDS, amphetamine level, age of participants, or duration of addiction at baseline (Table 7).

3.14. Serum urea and creatinine levels

Urea levels showed a positive significant correlation with the SDS, age of participants, and duration of addiction in groups II and III at baseline. In contrast, there were no significant correlations between urea and amphetamine levels in both these groups at baseline. Serum creatinine levels showed no significant correlations with SDS and amphetamine levels in groups II and III at baseline. creatinine levels were positively and significantly correlated with the age of the participants in groups II and III at baseline. Conversely, creatinine levels showed no significant correlation in group II and positive significant correlation in group III with duration of addiction at baseline (Table 7).

3.15. Serum oxidative stress biomarker levels

Serum MDA, GPx and CAT levels showed no significant correlation with SDS in groups II and III at baseline. The SOD activity was positively and significantly correlated with the SDS score in groups II and III at baseline. There were no significant correlations between MDA level and amphetamine level in group II and in contrast, levels showed a positive significant correlation in group III at baseline. MDA levels showed no significant correlation with age of participants or the duration of addiction in group II and showed a negative significant correlation in group III at baseline. SOD activity showed no significant correlation with amphetamine levels in group II and showed a positive and significant correlation in group III. SOD activity showed no significant correlation with the age of participants in groups II and III at baseline While, SOD score had negative significant correlation with the duration of addiction in group II and no significant correlation in group III. GPx levels showed a positive and significant correlation in groups II and III with the amphetamine level at baseline. In group II, there was no significant correlation between GPx level, age of participants and the duration of addiction, in contrast, group III showed a positive significant correlation at baseline. CAT activity showed no significant correlation with SDS in groups II and III at baseline. CAT activity was positively and significantly correlated with amphetamine levels in group II and showed no significant correlation in group III at baseline. Conversely, CAT level showed no significant correlation with the SDS, age of participants, or duration of addiction in both groups (Table 7).

4. Discussion

This study shows that the lack of female participants in this study could have been attributed to the strict socio-cultural environment surrounding the confidentiality of the cases. This limitation was reported recently in the Qassim region (Ibrahim et al., 2018), whereas another study showed that the percentage of female substance users was only approximately 12% in Riyadh (Alghamdi et al., 2016). These reports confirm the special circumstances surrounding evaluating SUD among females. Ridley and Coleman (2015) has also been reported that more than the half of the hospitalized patient was male in Albany, Western Australia. Saquib et al. (2020) reported that male sex was a significant risk factor for substance use disorder in KSA. This could be due to the following reasons: males have more freedom than females to go outside the home and to stay out late at night, they can go to rest areas and go on vacation with their peers more easily than females.

In Saudi Arabia, SUD is considered a major problem and the evidence of its association with psychiatric disorders, several diseases, serious educational and occupational losses, along with the associated socio-economic burden is well documented (Bassiony, 2013). This study showed that the age group mostly affected with amphetamine-related disorders was between 31 and 40 years old, whereas the age group mostly affected by amphetamine plus cannabis use was between 20 and 30 years old. Several reports have indicated a rise in SUD among the Saudi population. Almost 8% of Saudis at some point have reported using illicit substances (Saquib et al., 2020). In 2014, Sweileh et al. reported that amphetamine and cannabis use in Saudi Arabia had increased since the last decade. In accordance with these findings, a worldwide report indicated an upward trend in substance abuse among young users, of which amphetamine and cannabis are the most commonly used drugs (Ibrahim et al., 2018, Ridley and Coleman, 2015).

Moreover, this study indicated that most of the drug users were concentrated in urban areas, (Buraydah, Al-rass, Unayzah and Albukayriah). This is consistent with the results found by Pullen and Oser (2014). Conversely, Roche and McEntee (2017) demonstrated that significantly higher methamphetamine use is reported in rural and remote Australia compared to urban locations.

This study revealed that the marital status was mostly married in the amphetamine group while single in the amphetamine plus cannabis group. Angoorani et al., 2012 reported that body builders used amphetamine were married. In 2019, Alahmari et al. and in 2020, Saquib et al. reported separately that single status was linked to being cannabis users and other stimulants. These studies were consistent with our findings in amphetamine plus cannabis users while our findings in the amphetamine group showed mostly married users although there was a high percentage of individuals in the amphetamine group who were single. Most of the participants were living with their families, although other individuals also live with friends or alone for different circumstances such as a work or studying far away from their primary residence.

Regarding the educational level, in both the amphetamine and amphetamine plus cannabis groups, most participants had a Secondary school education, while a few were highly educated at the university level, only a few participants had no education. Recently, Ibrahim et al. conducted a study at Qassim rehabilitation center whose results were in line with this study finding (Ibrahim et al., 2018). Furthermore, in 2016, Al-Musa and Al-Montashri conducted a study in the Aseer region of Saudi Arabia among all secondary schools in Abha city, which revealed that 8.8% of students abused illicit drugs. Regarding the occupational level, the level of income was associated with the use of illicit drugs. This relationship was proportional to the monthly income of the users (Emara and Elgharabawy, 2009, Al-Musa and Al-Montashri, 2016). A novel finding of our study was the high percentage of amphetamine users who were unemployed (40%), which may be an indicator of potential criminal activities to obtain money to pay for illicit drugs (Abomughaid et al., 2018).

All the participants were smokers, caffeine users, and for the majority the duration of drug use for both user groups was more than 5 years. The same trend was reported in Qassim (Ibrahim et al., 2018), Moreover, we found that the influence of friends and the work environment played a role in the use of illicit drugs. Associated with the fact that most users were jobless, substance abuse could be associated with the need to escape the reality of the situation (Bamofleh et al., 2017).

It is well established that ATS reduce appetite and have been previously used for treating obesity (Stăcescu et al., 2019). Our results show that both the drug user groups had a significant reduction in BMI on admission and after the detoxification course in the hospital compared to the control group. Our study also indicated a significant increase in the heart rates of the drug users on admission before the treatment phase compared to heart rate after the detoxification. Our findings were consistent with the results of study conducted in King Abdul-Aziz Medical City in Riyadh between 2006 and 2013 (Alghamdi et al., 2016).

Amphetamine induced hyperadrenergic state that has a direct inotropic and chronotropic effect on cardiac muscles and vasoconstriction of the peripheral blood vessels. This state induces long term hypertension in amphetamine users (Duflou, 2019). Blood pressure, both SBP and DBP, on admission was significantly increased compared to controls and after the detoxification phase. This finding was compatible with a study conducted on Saudi patients who sought treatment for addiction in 2011 (Hennissen et al., 2017). Hurley et al., 2020 demonstrated that amphetamine impaired mRNA expression accompanied with neuroinflammation and activation of renin-angiotensin-aldosterone system in the lamina terminalis. This effect induced dysregulation in the sympathetic nervous system tone and blood pressure. This observation explains occurrence of hypertension in amphetamine users. Because ATS has effects on the cardiovascular system, this might place the addicts at a higher risk of cardiovascular complications such coronary syndrome, myocardial infarction, and myocarditis (Hennissen et al., 2017). ATS, and to a smaller extent cannabis, have been reported to be associated with many cardiovascular adverse effects and ATS cardiovascular-related adverse effects are the second leading cause of death in ATS users following accidental overdosing (Darke et al., 2017). ATS cause serious adverse effects on cardiac tissues promoting structural remodeling and electrical changes leading to potential fatal cardiac arrhythmia and heart failure (Kevil et al., 2019). In addition to ATS, growing evidence suggests the potential toxic effects of cannabis use on the cardiovascular system, of which an increase in blood pressure and heart rate, might trigger fatal complications (Subramaniam et al., 2019). However, these serious cannabis adverse effects seem to be observed only in high-risk populations (Volkow et al., 2014).

The RR for some participants in this study was significantly increased in the amphetamine and amphetamine plus cannabis group on admission compared to the control group. Similar results were obtained from previous studies on methamphetamine users, clarifying increased sympathomimetic effects as a possible explanation for such changes (Radfar and Rawson, 2014).

Cardiac TnT levels are the gold standard biomarkers for detecting cardiovascular-related injuries, such as myocardial infarction and acute coronary syndrome, as well as predicting clinical outcome (Riley et al., 2017). Our findings showed that TnT levels were significantly elevated at admission in the amphetamine and amphetamine cannabis group compared with the control group suggesting the presence of underlying cardiac toxicity when considered together with higher BP and heart rate observed in these individuals.

IgM is considered the first antibody to fight and clear new infections that might occur due to any reason, therefore, its first line of defense. Instead, IgG is the most abundant antibody found in blood and extracellular fluids. In this study, we measured serum IgM and IgG levels to help draw a general conclusion of immune system status of drug users (Chovancova et al., 2017). To determine the effects of ATS on the immune system, we measured the serum levels of IgG and IgM of drug users on admission and after treatment. IgM and IgG levels were significantly decreased on admission in both the drug user groups compared to the control group. Further, after the detoxification phase, the levels of IgM and IgG increased; however, these levels did not reach those of the control group. Our findings strongly coincide with previous reports indicating the potential detrimental effects of substance abuse/ATS on immunity. Wei and Shah (2020) reported that methylenedioxymethamphetamine suppresses humoral immunity responsiveness by decreasing the number T-cells, and these findings were further supported by Islam et al. in 2006. Further studies indicated that ATS immunosuppressive effects were not caused by direct drug effects on immune cells but could be attributed to the release of endogenous immunomodulatory substance. Studies by Boyle and Connor, 2010 reported the suppressive effects of ATS on immune functioning are mediated by catecholaminergic β-adrenoceptors and nicotinic acetylcholine receptors, which can increase susceptibility to infection and immune-related disorders, as shown in some cases of meningococcal meningitis linked to ATS usage (Bowyer and Hanig, 2014).

LH is a hormone released following stimulation by gonadotropin-releasing hormone (GnRH) from the anterior pituitary. It stimulates the production of TSTS from Leydig cells in the testes. In this study, we measured the serum levels of LH and TSTS hormone on admission and after detoxification. Both hormone levels were significantly increased in the drug user groups on admission compared to control while, after detoxification levels decreased from baseline values at admission but still remained elevated compared to control. This indicated an improvement in LH after cessation of use illicit drugs, although the levels might need extra time to reverse to normal values. In a study conducted by Dolatshahi et al., (2016), a relationship between methamphetamine use and sexual function was observed. The authors found enhance sexual desire, reduce behavioral inhibition, increase erection. These findings might be linked to the significant increase in gonadal hormone levels of drug users. There is an extreme shortage in studies conducted on humans regarding the clinical effects of illicit drugs on sexual function.

Cells ameliorate adverse effects of oxidative stress by many defense mechanisms to antagonist and stop cellular damage including non-enzymatic antioxidant such as vtamin C, Vitamin E and glutathione and enzymatic antioxidant such as superoxide dismutase, catalase and glutathione peroxidase (Draz et al., 2009, Deavall et al., 2012). The current study reported that amphetamine

users and amphetamine plus cannabis users on admission exhibited a significant increase in serum MDA, SOD, GPx, and CAT compared to healthy controls. In addition, we report here that MDA, SOD, GPx, and CAT test values after the 3-week detoxification treatment significantly decreased compared to their baseline values on admission; however, these did not reach levels of healthy controls. Our findings of increased levels of MAD, GPx, and CAT agree with a previous report showing enhanced oxidative stress markers among methamphetamine users (Huang et al., 2013). However, we show herein, there was an increased level of SOD activity at baseline, in contrast to their findings as well as to those of another report showing decreased erythrocyte SOD activity (Govitrapong et al., 2010). In addition, a post-mortem study examining the SOD activity in brain tissues of methamphetamine users reported an increase in its activity (Yamamoto and Raudensky, 2008). It is worth noting in our study, the specific compositions of the drug of abuse used was not identified and investigated. In addition, timing of measurements differed in our study, and the dose of substances used were reported. Thus, it is highly likely that different cellular adaptation might have occurred.

5. Limitations of the study

The limitation of this research is its cross-sectional design on short period of follow up to the participant. Other limitation is there is no evidence about the composition of illicit drugs that taken by the addicts. It needs Longitudinal study with more examination and confirmation of the addictive components by coordinating with Drug Control Department at the Ministry of Interior through following necessary requirements. Then working on prolonged program to treat a group of addicts through specialized advanced treatment center. Also, Ethical problems have surrounded prospective studies on the impacts of illicit drugs on humans due to the illegal nature of these substances and their harmful side-effects. The clear relationship between consumption and human health has become very difficult to construct.

6. Conclusions

The current results have shown the addiction of amphetamine and cannabis exert detrimental effects on different body organs and the exert major consequences on the health status of drug users. The present study showed that, there was no improvement in the levels of oxidative stress biomarkers, although an improvement was observed in the other parameters after the detoxification phase. The outcome of this work suggests that antioxidants plus standard treatment may contribute to optimizing treatment outcomes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

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