Republic of Iraq

Ministry of Higher Education and Scientific research

University of Babylon

College of Sciences

Department of Biology

Relationship of Addict Marijuana (THC) and Amphetamine (AMP) with Liver and Kidney Functions

A Research

Submitted to the College of Science/University of Babylon

in Partial Fulfillment of the Requirements for the

Degree of Higher Diploma in Science/ Forensic Evidences

By

Manar Jamil Kadhum Mohamed

(B.Sc. Biology / University of Kufa /2005)

Supervised by

Asst.Prof. Dr. Azhar Hamza Hassan

2021 AD **1443 AH**

بسم الله الرحمن الرحيم

﴿قالوا سبحانك لاعِلمَ لنا إلا ما علمتنا إِنَكَ أنتَ العِليم الحَكيمُ﴾

صدق الله العلي العظيم

سورة البقرة (آية 32)

Certification

I certify that this Research was prepared under my supervision at the Department of Biology, College of science, University of Babylon, as a partial requirement for the Degree of Higher Diploma of in Forensic Evidence.

Signature:

Name: Asst.Prof. Dr. Azhar Hamza Hassan

Data:

In view of available recommendation, I forward this thesis for debate

By the Examination Committee.

Signature:

Name: Asst. Prof. Dr. Adi Jassim Abd AL-Razzak

Title: Head of Biology Department.

Data:

Committee Certification

We, the examining committee, certify that we have read the thesis entitled (***Relationship of Marijuana(THC) and Aphetamin(AMP) addiction with Liver AND kidney function***) and examined the student (**Manar Jamil Kadhum Mohamed**) in its contents and that our opinion it is accepted as a thesis for a degree of high diploma in forensic evidences with (**Excellent**)degree.

Signature:

Prof.
Dr. Ali Hmood AL-Saadi

College of Science
University of Babylon
Date: / /2021
(Member)

Signature:

Prof.
Dr. Maysaa Adil Hadi

College of Science
University of Babylon
2021/ /Date:
(Chairman)

Signature:
Asst. Prof.
Dr. Azher Hamzah Hasan Kadhum
Depart of Biology
College of Science
University of Babylon
Date: / /2021
(Member and Advisor)

Approved by the College Committee of Graduate Studies.

Signature
Prof.Dr. Enass Mohammed Al-rubaie
Dean of College of Science Babylon University

Date: / /2021

Dedication

To my Lord, my supporter ……

To Prophet Muhammad and the pure infallible Imams,

my ultimate guide…

To my dear father, The kind heart my mother, the secret of my existence…

To my husband ….

To my brother and sisters…

To my country, my home and pride…

I dedicate this work.

Manar 2021

*A*cknowledgements

First of all, many thanks due to Allah, prophet Mohammed, Al- Emam Ali and his immaculate household for giving me the strength and patience in completing this work.

My sincere deepest thanks and my appreciation go to my supervisor **Asst.prof. Azhar Hamza Hassan** to pursue my work and for their great assistance during my study period till the end of the research.

Thanks to the University of Babylon, College of Science and Department of Biology for providing the necessary facilities during this study. In addition, I specially want to thanks to all patients that gave me their blood.

I specially want to thanks my close friends, Special thanks for all colleagues and many people who have played a key role in supporting my deplume research. I remain, deeply, grateful to all of them, and apologize to them for not being able to mention them by names.

Summary

This study was conducted to investigate the effect of Marijuana (THC) and Amphetamine (AMP) addiction on liver and kidney functions .

The study was carried out on (40) individuals of Addict Marijuana (THC) and Amphetamine (AMP) and 15 sample as a control group, The study lasted for three months for the period 23/5/2021 - 22/8/2021.This study was carried out at Al-Sadr Medical city, Najaf, the study aimed to study some side effects of the drugs which accompany this case of addiction. The study also aimed to identify the effect of abuse Marijuana (THC) and amphetamine (AMP) on function of liver and kidney. The biochemical (AST, ALT, ALP, Urea and Creatinine) changes which could happen to the addicts of such drugs.

It has been found that the use of abuse Marijuana (THC) and amphetamine (AMP) which effect on liver enzyme showed a significant increase ($P \leq 0.05$) in the group of abuse when compared to the control group (AST & ALT) in enzyme concentration , there is a significant increase in AST enzyme concentration (44.952± 3.67) when compare to control group (26.133± 1.38), While ALT enzyme concentration was also a significant increase ($P \leq 0.04$), higher ALT level in serum of addict group (52.717±5.414) when compares to control group (34.4±2.332), and the results of ALP enzyme showed a significant ($P \leq 0.001$*) increase in the effectiveness of the alkaline phosphatase enzyme in the patients (140.323±3.971) when compared with the control group (107.8 ±9.83) .

The result of kidney function showed there is a non-significant increase ($P > 0.05$) in the serum urea concentration of the group of drug users slightly increase (28.273±1.173) when compared to the control group (26.533±1.743) while the level of creatinine also showed a non-significant increase ($P > 0.408$) in

the blood serum creatinine of the in-abuse group (0.814±0.033) and (0.76±0.058) in the serum of the control sample.

The present results conclude from the current study that drug abuse affects liver and kidney functions and in the future leads to severe liver disease and kidney failure.

List of content

List of Table

List of Figures

List of abbreviation

abbreviation	Means
ALT	alkaline phosphatase
AMP	Amphetamine
BUN	blood urea nitrogen
CBD	Cannabidiol
CKD	Chronic kidney disease
CNS	Central nerves system
DFSA	drug facilitated sexual assault
FDA	Food and Drug Administration
GFR	glomerular filtration rate
LD	lactate dehydrogenase
MDA	Malondialdehyde
MIDMA	Methylenedioxymethamphetamine
NIDA	National Institute on Drug Abuse
NPN	non-protein nitrogenous
THC	Tetrahydrocannabinol

Chapter One

Introduction

1. Introduction

Drugs are considered as one of the main problems of the country's health and they caused the prevalence of some infectious diseases with a chronic and recurrent nature, which is threatening the health and human life. Addiction has engaged all industrial and nonindustrial societies along with malnutrition and environmental pollution (Pourallahvirdi *et al.*,2016). Rejections from friends, family relationships, loss of respect and occupation are included among the problems that can cause individuals to be addicted. Despite widespread tendency causes, preventive measures to reduce the damage caused by drug abuse have not well known yet (Lotfi *et al.*,2015).

Death associated with alcohol abuse and alcoholism now rank the third, behind heart disease and cancer (Al-khafaji,2010). The use of drugs in adolescents who their friends have a positive attitude towards drugs is higher, even up to two-thirds of the causes for using the drugs is how much close friends talk about the drugs, and a friend suggests them to accept the use of drugs (Kendler *et al*.,2014).

Marijuana is the most commonly used addictive drug after tobacco and alcohol, the marijuana plant has chemicals that can help with some health problems. More states are making it legal to use the plant as medicine for certain medical conditions. but there isn't enough research to show that the whole plant works to treat or cure these conditions. The U.S. Food and Drug Administration (FDA) has not approved the marijuana plant as a medicine. Marijuana is still illegal at the national level. However, there have been scientific studies of cannabinoids, the chemicals in marijuana. The two main cannabinoids that are of medical interest are Tetrahydrocannabinol (THC) and cannabidiol (CBD) (Wells and Ott,2011).

Amphetamine is a type of alkaloid, an organic compound. Amphetamine is a class of drugs that raise mood, energy, dopamine levels in the brain, and suppress appetite. They are also used to enhance mental and physical performance and to focus attention. Repeated use can lead to paranoia, delusions, and even psychosis. Among the physical side-effects are heart palpitations, arrhythmia and insomnia After cannabis, Amphetamine-type stimulants (ATS) are the second most widely used drugs across the globe outstripping the use of heroin or cocaine (Uddin *et al*., 2017).

Abuse of amphetamine (AMP) and its derivatives, such as 3,4-methylenedioxymethamphetamine (MDMA, 'Ecstasy'),3,4 methy lenedioxyethyl amphetamine (MDEA, MDE), and 3,4 methylenedioxyamphetamine (MDA) is an important public issue. Fatalities following ingestion of these substances are not infrequent in current forensic practice (De Letter *et al*.,2006).

Drug addiction has been associated with various forms of renal diseases which may be related to direct effect of the drugs themselves while others are caused by complications related to drug abuse (Kunis *et al*.,2008). Chronic use of some drugs, such as heroin, inhalants, and steroids (appearance- and performance-enhancing drugs), may lead to significant damage to the liver, this damage can be worse when these drugs are combined with alcohol or other drugs, in many cases, the liver is able to metabolize drugs (and other toxins) without significant damage to the organ itself. However, when persistent detoxifying demands are made of the hepatic system – for example, when drugs are taken in excess, when the frequency of drug use is on the order of daily or hourly, or when multiple substances are consumed simultaneously – drugs can cause significant, cumulative damage to the liver (Ramachandran, and Kakar, 2009).

Some drugs may cause kidney damage or failure, either directly or indirectly, from dehydration, dangerous increases in body temperature, and muscle breakdown. The pathophysiologic link between drug use and kidney disease is poorly defined. Potential renal injury occurs due to vasoconstriction and alteration of glomerular microcirculation via the actions of norepinephrine, endothelins, the renin-angiotensin-aldosterone system, and the L -arginine-nitric oxide pathway. cocaine has also been shown to increase oxidative stress and reduce intracellular glutathione in renal epithelial cells, thus, the exact mechanism of injury from cocaine and resulting pathology remains unclear (Norris *et al.*,2001).

1.2 Aim of this study

The aim of this study to use forensic serology to detect the effect of abuse Marijuana (THC) and amphetamine (AMP) on function of liver and kidney.

This performed by following objective:

1- Samples collection (urine and blood) from Addicts.
2- Identification of abuse by special kit (urine sample)
3- Estimation of liver enzymes (AST, ALT, ALP) in serum.
4- Estimation of Kidney functions (urea, creatinine) in serum.
5- Compare results.

Chapter Two

Literature Reviews

2.Literature Reviews

2.1 Abuse Substance

Drugs are chemicals which cause either physical or mental changes in body functioning. These chemicals may be natural, such as cocaine, semi synthetic, such as heroin and ecstasy, or totally synthetic, such as methadone. There is a perception that people use drugs for negative reasons -because they are depressed, unhappy, that most drug users get intense pleasure and enjoyment out of the drugs they consume. While most drug users take their drug for its mental effects, the drug is also affecting other parts of the body, thus physical effects are also part of the equation (Cone, 1995; Ho, and Lo,2019).

Generally, when most people talk about substance abuse, they are referring to the use of illegal drugs. Drugs of abuse do more than alter your mood. These drugs got to be illegal in the first place because they are potentially addictive or can cause severe negative health effects. Some believe the use of illegal substances is considered dangerous and, therefore, abusive, others argue that casual, recreational use of some drugs is not harmful and is merely use, not abuse. The most vocal of the proponents of recreational drug use are those who smoke marijuana. They argue that marijuana is not addictive and has many beneficial qualities, unlike the "harder" drugs. But recent research has shown that even marijuana may have more harmful physical, mental, and psychomotor effects than first believed. Each year, new scientific studies find more ways that long-term marijuana use is harmful to your health (Csete *et al*.,2016).

In addition, the National Institute on Drug Abuse (NIDA) reports that marijuana users can become psychologically dependent, and therefore addicted. NIDA

estimates that one in every seven users of marijuana becomes dependent (Rai and Winder,2017).

2.2 Addiction

Drug addiction has become a worldwide problem and the leading cause of death. The global problem of addiction and drug abuse is responsible for hundreds of deaths every year. It affects not only individual users, but also their families and communities, addiction, or to give its jargon term, drug dependence, is the compulsive use of a drug on a regular basis in order to experience its psychoactive effects or to avoid the discomfort of its absence. There are different types of dependence, i.e., dependence on the opiate type, dependence on the alcohol type and so on. Many drugs result in compulsive use after repeated exposure to them. Examples include heroin and other opiates, alcohol, tranquillizers, nicotine, cocaine. Sometimes the dependence is physical, sometimes it is psychological. The latter is the most difficult to deal with. Addictive use is the most serious problem a drug user can face because it often means daily exposure to the drug (Obot and Room2005).

2.3 Types of drugs

2.3.1 Cocaine

Hydrochloride is a psychoactive substance extracted from the leaves of plants called Erythroxylon coca. Cocaine is a potent stimulant of the sympathetic nervous system and causes structural changes on the brain, heart, lung, liver and kidney (Manetti *et al*.,2014).

Effects: of cocaine may therefore vary depending on dosage, frequency of use, individual response and prior health status. Cocaine is a potent stimulant of the sympathetic nervous system and causes irreversible structural changes on the brain,

heart, lung and other organs such as liver and kidney (Mitchell,2006).The cardiovascular effects (atherosclerotic phenomena, coronary arteries vasoconstriction, thrombus formation… act (Manetti, 2014).

2.3. 2 Alcoholic

Beverages have been a part of social life for millennia, yet societies have always found it difficult to understand or restrain their use, Alcohol's combined effects on both innate and adaptive immunity significantly weaken host defenses, predisposing chronic drinkers to a wide range of health problems including infections and systemic inflammation. Alcohol consumption does not have to be chronic to have negative health consequences (Oye, 2007).

In fact, research shows that acute binge drinking also affects the immune system. There is evidence in a number of physiological systems that binge alcohol intake complicates recovery from physical trauma, alcohol impairs recovery from three types of physical trauma burn, hemorrhagic shock, and traumatic brain injury by affecting immune homeostasis The combined effect of alcohol and injury causes greater disruption to immune function than either challenge alone , alcohol exposure, and particularly chronic heavy drinking, affects all components of the adaptive immune system. Studies both in humans and in animal models determined that chronic alcohol abuse reduces the number of peripheral T cells, disrupts the balance between different T-cell types, influences T-cell activation, impairs T-cell functioning, and promotes T-cell apoptosis. Chronic alcohol exposure also seems to cause loss of peripheral B cells, while simultaneously inducing increased production of immunoglobulins (Sarkar *et al*.,2015).

In particular, the levels of antibodies against liver-specific auto antigens are increased in patients with alcoholic liver disease and may promote alcohol-

related liver damage. the chronic alcohol exposure in uterus interferes with normal T-cell and B-cell development, which may increase the risk of infections during both childhood and adulthood, alcohol's impact on T cells and B cells increases the risk of infections (e.g., pneumonia, HIV infection, hepatitis C virus infection, and tuberculosis), impairs responses to vaccinations against such infections, exacerbates cancer risk, and interferes with delayed-type hypersensitivity. In contrast to these deleterious effects of heavy alcohol exposure, moderate alcohol consumption may have beneficial effects on the adaptive immune system, including improved responses to vaccination and infection. The molecular mechanisms underlying ethanol's impact on the adaptive immune system remain poorly understood (Pasala *et al*., 2015).

Alcohol use could relate to an increased risk of homicide victimization in several ways. Alcohol could increase the likelihood of risk-taking and provocative behavior by some potential victims; this might, in turn, lead to violent interactions and homicide, alcohol which, acting as a central nervous system depressant, may release inhibitory control mechanisms and thereby permit expression of aggressive or violent behavior. Alternatively, individuals who are intoxicated may be easier targets for robberies and other predatory crimes that often end in homicide, clinical and experimental research has addressed the questions of whether alcohol use increases risk-taking behavior, whether behavioral effects of alcohol are modulated by the presence of congeners, and whether alcohol use and instigator intent are important in shaping aggressive behavior (Friedman *et al*.,2006).

Regarding the role of alcohol in crime victimization, approximately 3 million violent crimes occur each year in which victims perceive the offender to have been drinking at the time of the offense. Approximately half the incidents described by

the investigating officer as alcohol-related were between offenders and victims who were intimates (Nolan *et al.*,2017).

2.3.3 Heroin

Heroin is an opioid drug made from morphine, a natural substance taken from the seed pod of the various opium poppy plants grown in Southeast and Southwest Asia, Mexico, and Colombia. Heroin can be a white or brown powder, or a black sticky substance known as black tar heroin. Other common names for heroin include big H, horse, hell dust, and smack (NIDA, 2018).

Heroin is one of the more common illicit drugs used around the world, often in combination with other drugs that depress the central nervous system. Repeated use of heroin leads to a dependence and tolerance requiring higher doses to achieve the desired pharmacological effect. The risk of sudden death is high, particularly if used with other drugs. Blood concentrations of the active metabolite morphine is poorly correlated with toxicity. Repeated use of heroin can lead to significant ill-health and injury, and sudden death (Rafaiee *et al*.,2013).

2.3.4 Ecstasy

MDMA(n-methyl-3,4-methylenedioxymethamphetamine), also known as ecstasy, is a psychoactive drug used for leisure described as having stimulating and hallucinatory effects. These effects stem from its action in the central nervous system, raising extracellular serotonin and dopamine (Almeida and Silva ,2003).

Risks most legal drugs are tested on animals first, but ecstasy users are human guinea pigs. Research already shows that regular weekend users experience

a mid-week ‘crash’ that can leave them feeling tired and depressed, often for days. It could be years before we know the long-term effects but some users may be at risk of developing mental health problems later in life. Deaths from ecstasy are quite rare, but can be due to heatstroke, heart attacks or asthma attacks (Kiyatkin,2014).

2.3.5 Amphetamines

Amphetamine is a type of alkaloid, an organic compound. Amphetamine is a class of drugs that raise mood, energy, dopamine levels in the brain, and suppress appetite. They are also used to enhance mental and physical performance and to focus attention. Repeated use can lead to paranoia, delusions, and even psychosis. Among the physical side-effects are heart palpitations, arrhythmia and insomnia After cannabis, ATS are the second most widely used drugs across the globe outstripping the use of heroin or cocaine (Uddin, *et al*., 2017).

Amphetamine was discovered over 100 years ago. Since then, it has transformed from a drug that was freely available without prescription as a panacea for a broad range of disorders into a highly restricted Controlled Drug with therapeutic applications restricted. amphetamine’s diverse pharmacological actions translate not only into therapeutic efficacy, but also into the production of adverse events and liability for recreational abuse. Accordingly, the balance of benefit/risk is the key challenge for its clinical use. , which is the first d-amphetamine prodrug approved for the management of ADHD in children, adolescents and adults. The unusual metabolic route for lisdexamfetamine to deliver d-amphetamine makes an important contribution to its pharmacology (Heal *et al.*,2013).

The effects of amphetamines and methamphetamine are similar to cocaine, but their onset is slower and their duration is longer. In contrast to cocaine, which is quickly removed from the brain and is almost completely metabolized, methamphetamine remains in the central nervous system longer, and a larger percentage of the drug remains unchanged in the body, producing prolonged stimulant effects (Sinha *et al*., 2016).

Chronic abuse produces a psychosis that resembles schizophrenia and is characterized by: Paranoia, picking at the skin, preoccupation with one's own thoughts, and auditory and visual hallucinations. Violent and erratic behavior is frequently seen among chronic abusers of amphetamines and methamphetamine (Blickman, 2011).

2.3.5.1 Clinical implications of amphetamine

The primary action of amphetamine is to increase synaptic concentrations of monoamine neurotransmitters, thereby indirectly enhancing noradrenergic, dopaminergic neurotransmission in the CNS. Although amphetamine's isomers are also powerful 5-HT-releasing agents in vivo (Heal *et al.*, 1998; Kuczenski *et al.*,

1995). this action does not appear to contribute to their efficacy in treating ADHD. This opinion is based on clinical experience with fenfluramine, which is a chemical analogue of amphetamine and a powerful releasing agent with a preferential action on 5-HT (Tao et al., 2002).

Donnelly *et al.* 1989) reported that fenfluramine was not effective in treating the disruptive and overactive behaviors in ADHD; nor did it ameliorate the conduct disorder that was present in about half of the subjects. However, it is possible that the actions of amphetamine to increase serotonergic drive may have a beneficial effect on anxiety or depression that is often comorbid with ADHD. Thus, enhanced

catecholaminergic signaling is the primary mediator of amphetamine's efficacy in ADHD and narcolepsy. On the negative side, the same pharmacology is also responsible for amphetamine's major side effects and also its liability for recreational abuse. Therefore, optimizing therapeutic efficacy whilst simultaneously maintaining side effects at an acceptable level is a difficult balance requiring careful dose titration in the patient (Easton *et al*.,2007).

2.3.6 Marijuana

also called weed, herb, pot, grass, bud, ganja, Mary Jane, and a vast number of other slang terms—is a greenish-gray mixture of the dried flowers of Cannabis sativa. Some people smoke marijuana in hand-rolled. The main psychoactive (mind-altering) chemical in marijuana, responsible for most of the intoxicating effects that people seek, is delta-9-tetrahydrocannabinol) THC). The chemical is found in resin produced by the leaves and buds primarily of the female cannabis plant, effects of cannabis produce euphoria and relaxation, perceptual alterations time distortion, and the intensification of ordinary sensory experiences, such as eating, watching films, and listening to music (Petit *et al*., 2012).

Cannabis can effect on memory and concentration and made body tired and lacking motivation. Many people consider cannabis to be a relatively safe drug. But research shows that long-term users can find it hard to control their use of the drug and may become addicted. Smoking cannabis increases the risk of heart disease and cancers such as lung cancer and may also affect the fertility. In people who have underlying mental health problems, cannabis use may trigger schizophrenia. In Ireland itis the second most common drug found in the systems of drink drivers, after alcohol.

Research has shown that marijuana's negative effects on attention, memory, and learning can last for days or weeks after the acute effects of the drug wear off, depending on the person's history with the drug. Consequently, someone who smokes marijuana daily may be functioning at a reduced intellectual level most or all of the time. Considerable evidence suggests that students who smoke marijuana have poorer educational outcomes than their nonsmoking peers (NIDA 2014).

Marijuana is unsafe for who driving wheel. Marijuana impairs judgment and many other skills needed for safe driving: alertness, concentration, coordination, and reaction time. Marijuana use makes it difficult to judge distances and react to signals and sounds on the road. (Hall and Solowij, 1998).

Marijuana is the most commonly identified illegal drug in deadly crashes, sometimes in combination with alcohol or other drugs. By itself, marijuana is thought to roughly double a driver's chances of being in a crash, and the combination of marijuana and even small amounts of alcohol is even more dangerous—more so than either substance alone (Volkow et al., 2014).

2.3.7 Inhalant abuse.

Is a prevalent and often overlooked form of substance abuse in adolescents and young adults. It causes a euphoric feeling, may become addictive and can be a serious health concern associated with significant morbidity and mortality. Acute effects of inhalants include sudden sniffing death syndrome, asphyxia, and traumatic injuries, chronic inhalant abuse can damage the brain, heart, lung, kidney, liver, and bone marrow in addition to being an important cause of psychosocial and economic problems (Tulsidas, 2010).

Inhalant abuse refers to the inhalation of volatile substances which produce euphoric effects. Commonly abused inhalants are hydrocarbons and anesthetic agents. Glues and adhesives are frequently abused as they are easily available and inexpensive, benzene and toluene are the chemical constituents in glues. Toluene methylbenzene, toluol, and phenylmethane) is an aromatic hydrocarbon (C7H8) which is commonly used as an industrial solvent in the manufacture of gasoline, acrylic paint, varnish, paint thinner, adhesive, glue, rubber cement, and shoe polish. At first, the most common substance inhaled was a toluene-based adhesive and therefore the term ‘‘glue sniffing’’ was soon given to this habit, though many of the substances now used are not adhesives, the more accurate title of ‘‘solvent abuse’’ has now been applied to this widespread and dangerous habit. (i.e. spraying paint into a plastic bag and inhaling, other methods of inhalational abuse are dusting spraying an inhalant directly in mouth or nose, glading inhaling air freshener aerosols sprayed in a room), and sniffing inhaling directly from the neck of a container (Jayanth *et al*., 2017).

The risks were death from solvent abuse is rare but it can happen for a number of reasons and can happen the first time do it. Under the influence of solvents more likely to have accidents. You may also choke or suffocate – on the solvent spray into lungs, on vomit or on the materials you use to help inhale the solvent. Many solvents can also cause heart failure (Singh, *et al*. 2009; Manetti *et al*., 2014).

2.3.8 Opioid.

Are a class of drugs that include the illicit drug heroin as well as the licit prescription pain relievers oxycodone, hydrocodone, codeine, morphine, fentanyl and others. Opioids are chemically related and interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain (Pouget *et al.*,2015).

Opioid induced side effects such as nausea, constipation, tolerance and addiction are widely known, but new detrimental effects are emerging in the clinical setting as well as in literature. They include hypogonadism, osteoporosis, immune suppression, cognitive impairment and hyperalgesia (Clarke *et al.,* 2014).

2.3.9 Stimulants.

The stimulants are any substance which increases or quickens a vital process. Within the central nervous system (brain and spinal cord), stimulants increase alertness, relieve fatigue, reverse cataplexy (muscle weakness), and/or induce euphoria. Outside the brain and spinal cord, stimulants frequently activate the sympathetic nervous system (Faraone *et al*.,2008).

Stimulation of this nerve highway prepares the body for "fight or flight" by dilating the pupils, increasing heart rate, and raising blood pressure. For example, many stimulants have direct effects upon dopamine and norepinephrine (catecholamines). Other stimulants, such as caffeine and nicotine, influence dopamine indirectly. (Jackson, 2009).

2.4 Abuse substance with crime

2.4.1 Sexual violence

Is defined as, “any sexual act, attempt to obtain a sexual act, unwanted sexual comments or advances, or acts to traffic women’s sexuality, using coercion, threats of harm or physical force, by any person regardless of relationship to the victim, in any setting, including but not limited to home and work (Nymoen *et al.*,2019).

According to this definition, a very wide range of behaviors, from rape at gun-point to sexual coercion under a threat of dismissal (i.e. with false agreement),

would be classed as an act of sexual violence. Sexual violence is a reality for millions of people worldwide, and for women in particular. Research indicates that the vast majority of victims of and for women in particular. Research indicates that the vast majority of victims of sexual violence are female, most perpetrators are male (Resnick *et al.,* 2013).

Sexual violence can happen to anyone, regardless of age, race, income level, ethnicity, religion, sexual orientation and education level. However, certain vulnerabilities or risk factors contribute to sexual violence victimization and perpetration; consuming alcohol and drugs is among those factors (Bonomi *et al*.2007).

Substances may have been used by the perpetrator to facilitate a sexual assault. Someone may have been using or abusing substances before an assault occurred, or started using substances as a coping strategy following an assault. Substance abuse and sexual victimization both carry a great deal of social stigma in and of themselves, and when a victim/survivor holds both, the stigma can be especially difficult to overcome. This stigma can compound the challenges of the healing process and increase feelings of blame, shame and isolation (Al-Hemiary and Talib, 2010).

Rape or other types of sexual assault are referred to as drug facilitated sexual assault (DFSA). In DFSA cases, the victim is subjected to a sexual act without legal consent as a result of the pharmacological effects of alcohol and/or drug(s). a large number of psychoactive substances have the potential to alter the victim's state of mind, alcohol being the number one candidate because of its widespread use, illicit drugs, psychoactive prescription drugs and even over-the-counter medicines are also likely candidates, either consumed alone or in combination with alcohol. The resulting pharmacological effects may include relaxation, euphoria,

and lack of inhibition on the one hand and drowsiness, loss of motor function, unconsciousness, and amnesia on the other hand. Information on the frequency of DFC cases is scarce but there has been a significant increase in reports worldwide (LeBeau, 2008).

However, several factors complicate the registration of the actual number of DFSA cases. Governmental statistics show a general underreporting of sexual assault crimes. The impact that central nervous system depressant drugs have on memory and consciousness might lead to a situation where the victim is not able to remember what has actually happened and chooses not to report the incident. If the incident is reported, police officers often assume that the victim was simply drunk rather than drugged. (Fernández**,** *et al*., 2014).

2.4.2 The relationship of traffic accidents with drugs

Traffic crashes are a common cause of death in many countries. Among the numerous risk factors (eg, speed, alcohol, talking on cell phones, road infrastructures), the effect of medicinal drugs has not received sufficient attention. Assessment of effects of medicinal drugs on driving ability by laboratory tests, driving simulators or on-the-road driving tests provides helpful insights on potential impact, but only partially assesses the impact in "real life" conditions where driver behavior, health status, and road traffic environment interact. Reports on the state of knowledge about drugs and driving were published in 1999 and 2003, showing an increase concern about the role medicinal drug use may play in road traffic crashes. In 2003. European Safety Action program was set up to encourage research on the effects of medicinal drugs, in order to establish a European classification regarding road safety (Orriols *et al*.,2009).

Impaired driving involving alcohol, illegal and legal drugs cause, each year, a great number of traffic accidents all over the world. alcohol is a recognized leading contributor to road accidents and the association between alcohol and traffic accident risk has been extensively demonstrated (Ravera *et al.*, 2011).

2.4.3 Relationship between drug abuse and Robby.

There is a close relationship between drug abuse and crime. Drug abusers commit crimes to pay for their drugs and this inflicts damages to the society. Moreover, many criminals are under the influence of drugs while committing crimes. Drug trafficking is another outcome of drug abuse (Rafaiee *et al*.,2013).

Crime related to drug abuse is mostly non -violent and often petty. Economic-compulsive crime to obtain drugs, such as theft and burglary, is more common than violent drug-induced assault. However, the impact of illicit drugs, crime and violence is highly damaging to local communities. Also, many crimes committed by substance users are categorized as drug crimes, as they involve either the use or handling of illicit drugs, or as acquisitive crimes such as stealing, shoplifting, or burglary, related to the need to finance drug use. For example, acquisitive crimes committed by drug users appear to decrease after substance use disorder treatment. Perpetrators of violent crime may differ from subjects committing these other drug-related crimes and may display different treatment needs (Håkansson and Jesionowska,2018).

2.5. Forensic serology.

Forensic Serology is the technology can be defined as the tools or methods used to apply this scientific knowledge. accurate and sensitive serological testing has become more valuable than ever as a means of providing forensic investigators with critical context for interpreting DNA test results, in addition, serology also

has significant utility as a gateway through which evidence can be efficiently screened as a prerequisite to subsequent genetic individualization. In this capacity, it helps to maximize the efficient use of laboratory and law enforcement resources Serology is such a convenient diagnostic tool because the immune system produces specific molecular tags in the blood for practically each foreign substance or invading microorganism, each one specializes in binding to a specific molecule such as a viral, parasite, or bacterial protein, as well as to foreign substances such as poisons and drugs (Jackson and Jackson, 2008).

For minutely small drug molecules against which the immune system is not very sensitive, special immune reagents were developed for the detection of drug abuse. An example is the Homogeneous Enzyme Immunoassays (EMIT), which is commercialized in kits ready for use. (Legg *et al*.,2017).

The study and examination of bodily fluids that is used in forensic science as a means of segregating fluids excreted by assailants or attackers in varying criminal acts. These acts can range from physical assault to sexual assault, right through to the act of murder and all of them will have an element of fluid secretion attached to them. Serology allows the forensic scientists to segregate these bodily fluids when found at the scene of the crime and then perform a variety of tests on them in order to identify where these fluids originated from - or most importantly - who they came from. One important aspect of Serology is determining whether or not stains resembling blood found at a crime scene are actually blood or some other stain that bears a similar resemblance, bodily fluids and their stains are useful biological evidence for forensic, serological, and DNA analysis and may be useful in solving crimes. The most common bodily fluids in forensic analysis are blood, seminal fluid, and saliva. Bodily fluid stains are commonly associated with violent criminal cases (LI. ,2015).

2.6. The identification of blood

Is important in many cases submitted to the crime laboratory for analysis. Blood identification is central to many homicide investigations and is also useful in cases involving aggravated assault, sexual assault, and burglary. The evaluation of blood evidence can be crucial to substantiate a complainant's or suspect's account of alleged events. The presence of blood on evidentiary items can be critical in establishing guilt or innocence during criminal proceedings (Muro and Lednev, 2017).

The analysis of blood evidence can be important not only in establishing which individual might have been bleeding, but also in the manner in which blood was deposited. Blood spatter interpretation can be valuable in determining how blood was deposited on an item or at a scene, thus making it useful in crime scene reconstruction. All of these factors can be taken into account during the investigation and prosecution of a crime and may corroborate or refute an individual's account of an assault (Zhang *et al*.,2017).

2.7 Liver enzymes

Liver enzymes play an important role in the assessment of liver function because injury to the liver resulting in cytolysis or necrosis will cause the release of enzymes into circulation. Enzymes also play an important role in differentiating hepatocellular (functional) from obstructive (mechanical) liver diseases, which is an important clinical distinction because failure to identify an obstruction will result in liver failure if the obstruction is not rapidly treated. Although many enzymes have been identified as useful in the assessment of liver functions, the most clinically useful enzymes are aminotransferases (alanine aminotransferase

[ALT] and aspartate aminotransferase [AST]), the phosphates (alkaline phosphatase [ALP] and 5-neucleotidase), -glutamyl transferees (GGT), and lactate dehydrogenase (Bishop and McCaughan ,2001).

2.7.1 Tests for liver function

Clinical laboratories offer several tests for assessment of liver function. The enzymes alkaline phosphatase, ALT, AST, GOT, GPT and 5′-nucleotidase are helpful in the assessment of the proper functioning and inflammatory status of the liver. Since the liver is the site for metabolism of carbohydrate, protein, and lipids, as well as for the synthesis of many proteins, the conjugation of bilirubin, and detoxification of drugs and other substances (Harris, 2005).

The liver may be assessed by measurement of total and direct bilirubin, total protein and albumin, cholesterol and triglycerides, and urea and ammonia. In this case, increased levels of enzymes and bilirubin and lowered protein are correlated with liver diseases. The extent of the increased alkaline phosphatase and the presence of high level in both total and direct bilirubin help to specify this liver disorder as obstructive jaundice (Arneson and Brickell ,2007).

2.7.2 Pathophysiology of liver enzymes

Enzyme's analysis is used to aid in diagnosis and treatment of diseases. In particular, enzymes that are synthesized within cellular organelles and carry out their functions within cells and are released into body fluids when those cells are damaged. Thus, an increase in enzyme activity when compared to the reference range can indicate pathological changes in certain types of cells and tissues. Enzyme's activity levels in body fluids can reflect leakage from cells due to cellular injury, or changes in enzyme production rate or actual enzyme induction due to metabolic or genetic states or proliferation of neoplasms (Lai *et al.*,2013).

Some enzymes are present in the plasma due to tissue necrosis or inflammation and increase at such a 10 slow rate that they are not useful for early detection or treatment of the disease. Other enzymes rapidly decline in circulation because of inactivation or metabolism. The clinical utility of enzyme activity in relationship to specific tissue pathology and clinical signs is enhanced when the enzyme activity quickly rises following the onset of the disorder and remains elevated for an adequate time frame, particularly when other clinical signs and symptoms are not sufficient to provide diagnosis. Damage to tissue can release different types of enzymes based on their location. For example, mild inflammation of the liver reversibly increases the permeability of the cell membrane and releases cytoplasmic enzymes such as lactate dehydrogenase (LD), alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST), while cellular death (necrosis) will release mitochondrial sources of ALT and AST (Yang *et al*.,2007).

Distributions of these enzymes within specific types of hepatic tissues varies. ALP and gamma glutamyl transferees (GGT) are more concentrated in the biliary ducts or tissues of the small ducts (canaliculi), while AST, ALT, and LD are present mainly in structural (parenchymal) hepatic cells. Multiple forms of enzymes, called isoenzymes, are distributed in several different tissue types. For example, ALP is found in hepatobiliary tissues but also present in all cytoplasmic membranes of all cells of the body, especially in osteoblasts (bone forming cells), intestinal mucosa, placenta, and renal tubules (Arneson and Brickell ,2007).

2.7.3 Effect abuse substance on Liver Function

Chronic use of some drugs, such as heroin, inhalants, and steroids (appearance- and performance-enhancing drugs), may lead to significant damage to the liver. This damage can be worse when these drugs are combined with alcohol or other drugs, Cannabis (marijuana) is the most commonly used illicit substance worldwide with an estimated 200 million users there is a strong association between cannabis abuse and abuse of alcohol, opiates, stimulants and sedatives, population-based study in the United States, found high prevalence of cannabis use in patients with schizophrenia, mania, panic disorder and major depression (Degenhardt *et al.*,2001).

Cannabis abuse does not cause acute hepatotoxicity. However, a study of 272 untreated patients with Hepatitis C demonstrated that daily cannabis smoking is a risk factor for progression of liver fibrosis, daily cannabis use was an independent predictor of rapid fibrosis progression rate (>0.15) (OR 3.6 [1.5–7.5]). Furthermore, severe fibrosis (Metavir score >F3) was also predicted by daily cannabis use independent of Metavir activity grade, alcohol consumption, age, steatosis and cigarette smoking. Cannabis smoking post liver transplantation anecdotally has been associated with severe recurrent HCV disease (personal observation) (Salo et al.,2011).

Amphetamine type stimulants (ATS) include the ‘amphetamine group’ comprising amphetamine and methamphetamine, and the ‘ecstasy group’ comprising 3,4-Methylenedioxymethamphetamine (MDMA). ATS can be smoked,

snorted, injected or ingested as suggested by the World drug report 2012, ATS (excluding ecstasy) were the second most commonly abused drugs worldwide in 2010 with an estimated prevalence of 0.3–1.2% globally among the population aged 15–64 ,global use of 'ecstasy group' substances is 0.2–0.6 % in the same age group, a study looking at 189 patients with methamphetamine dependence found 28% patients have primary psychiatric disorder and 32% patients had primary mood disorder ,Parenteral ATS abuse poses a high risk for exposure to Hepatitis C virus (HCV). A recent study from China found that 43% ATS users were exposed to HCV (Gray *et al*.,2012).

The effects of ATS can vary from acute hepatitis to ALF. Ecstasy induced hepatotoxicity can manifest, up to four weeks after ingestion, as mixed hepatitis. ATS use can lead to exhaustive dancing at hot night club 'raves' leading to heat stroke-like syndrome causing hyperthermia, shock, ischemia and hepatic necrosis [70]. A case series of seven patients who ingested ecstasy in nightclub, three patients had severe hepatotoxicity with two patients dying within four days of hospital admission with ALF, the exact mechanism of amphetamine induced liver injury remains unknown. Amphetamines undergo extensive hepatic metabolism largely by the hepatic P450 system (CYP 2D6) and generation of a toxic metabolite may be the cause of hepatic injury (Greene *et al*.,2003).

2.8. Kidney function test

Urea and creatinine are waste products produced during protein metabolism. Both of these waste products are carried to the kidney and filtered into the urine. They are measured to evaluate how well the kidney is working, Urea, commonly referred to as blood urea nitrogen (BUN) when measured in the blood, is a product of protein metabolism. BUN is considered a non-protein nitrogenous (NPN) waste product. Amino acids derived from the breakdown of protein are deaminated to

produce ammonia. Ammonia is then converted to urea via liver enzymes. Therefore, the concentration of urea is dependent on protein intake, the body's capacity to catabolize protein, and adequate excretion of urea by the renal system (Burtis, and Bruns, 2014).

Urea accounts for the majority (up to 80%–90%) of the NPNs excreted by the body. The body's dependency on the renal system to excrete urea makes it a useful analyte to evaluate renal function. An increase in BUN can be the result of a diet that is high in protein content or decreased renal excretion. Creatinine, also a NPN waste product, is produced from the breakdown of creatine and phosphocreatine and can also serve as an indicator of renal function. Creatine is synthesized in the liver, pancreas, and kidneys from the transamination of the amino acid's arginine, glycine, and methionine. Creatine then circulates throughout the body and is converted to phosphocreatine by the process of phosphorylation in the skeletal muscle and brain. The majority of the creatinine is produced in the muscle. As a result, the concentration of plasma creatinine is influenced by the patient's muscle mass. Compared to BUN, creatinine is less affected by diet and more suitable as an indicator of renal function (Price and Finney, 2000).

2.8.1 Clinical Significance

The measurement of creatinine concentrations in plasma and urine samples illustrates the filtration capacity of the glomerulus, also known as the glomerular filtration rate (GFR.) Creatinine is produced endogenously within the body and is freely filtered by the glomerulus. These characteristics make creatinine a useful endogenous marker for creatinine clearance. If the GFR is decreased, as is in renal disease, creatinine clearance via the renal system is compromised. The reduced

GFR will then lead to an increase in plasma creatinine concentration. The measurement of plasma alone should not be used to assess renal function. Plasma creatinine levels may not be affected until significant renal damage has occurred (Laterza *et al*.,2002).

In addition, a plasma creatinine level that is within normal reference range does not equate to a normal functioning renal system, although not as specific as creatinine, BUN can also be used as an indicator of renal function. BUN is not the preferred marker for clearance because it is influenced by factors such as a high protein diet, variables in protein synthesis, and patient hydration status. Alone BUN is not the ideal marker for GFR. Combined with plasma creatinine as a creatinine/BUN ratio, BUN can be a useful analyte in differentiating pre or post renal increase of plasma NPNs (Salazar, 2014).

2.8.2. Effect abuse substance on Kidney Function

There are numerous medical consequences to recreational drug use. Thus, physicians should consider substance abuse in any unexplained illness. The majority of these drugs, or their metabolites, are excreted via the kidney. While some substances may be directly nephrotoxic, a number of other mechanisms are also involved. To achieve their recreational effects these drugs must cross the blood-brain barrier and many are highly lipid-soluble; this results in high volumes of distribution with dialysis of little benefit in overdose. CKD (chronic kidney disease) is a major public health challenge, globally, 226 million men (10%) and 272 million women (12%) had CKD in 2010 (Mills *et al*.,2015).

In 2015, CKD accounted for 1.2 million deaths worldwide, representing a 32% increase from 2005 ,in developed countries, CKD is associated with older age,

diabetes, hypertension, obesity, and cardiovascular disease ,other studies have implicated several behavioral risk factors in the development or progression of CKD, including tobacco, alcohol, and illicit drug use, all of which may exhibit direct or indirect nephrotoxic effects, However, these modifiable risk factors and their associations with progression of CKD and all-cause mortality have not been well studied among patients with preexisting CKD (Orth and Hallan, 2008).

Harmful associations of addiction with many chronic diseases, especially cancer and cardiovascular disease, have been well documented ,although tobacco smoking has been associated with higher risk of incident CKD, the existence of an independent relationship with CKD progression has been questioned, especially among patients with preexisting CKD ,Similarly, although alcohol use has been associated with lower risk of cardiovascular disease and incident CKD ,its associations with CKD progression remain unclear. Furthermore, the association between illicit drug use and CKD progression is largely unknown. Recently, there has been increasing interest in decriminalization or legalization of use of illicit drugs, particularly marijuana, with more than one half of United States states currently allowing recreational and/or medicinal use of marijuana. Use of tobacco, alcohol, and illicit drugs may play a role both in the progression of CKD and death among patients with CKD (Anderson *et al.*,2012).

Drug abusers are becoming aware of the risk of dehydration and often drink large quantities of water after taking amphetamines to try to prevent this, as a consequence, cases of hyponatraemia, catatonic states and cerebral oedema have occurred, the dilutional hyponatraemia, due to excessive fluid ingestion, may involve inappropriate antidiuretic hormone secretion, ‘Chill out’ rooms are now provided in an attempt to prevent hyperthermia (Crowe *et al*.,2000).

In the USA, Amphetamines has not been taken as a dance drug and consequently the spectrum of unwanted effects is different, with cardiac arrhythmias being more common, a s ecstasy has marked sympathomimetic effects, it is not surprising that cases of accelerated hypertension with associated acute renal failure have been described. Similarly, urinary retention due to bladder neck closure has been associated with its use (Stark *et al*.,2019).

The abuse of substances both causes, and exacerbates, a wide spectrum of kidney disease. Increasingly, and unfortunately, drug abuse now must be considered in the differential diagnosis of any patient with unexplained renal pathology. Provision of dialysis for both acute and chronic renal failure is extremely costly, and this adds extra impetus to educational measures which serve to reduce substance abuse in the community (Alhamad et al.,2019).

Chapter Three

Materials and Methods

3. Materials and Methods

3.1. Equipment, laboratory tools and chemicals

Many equipment, laboratory tools and chemicals were used in the present study and they are summarized in tables (3-1 and 3-2).

Table (3-1): Chemicals used during this study

Items	Manufacturer
ALT kit	Biolabo
Creatinine kit	Epson LX-300/Italy
GOT kit	Biolabo
GPT Kit	Biolabo
Urea	Biolabo

Table (3-2): Equipment and laboratory tools used during this study

Items	Manufacturer
Autoclave	Haramaya/ Japan
Centrifuge	Hettich
Cool box	International Haotian Technology/ Chine
Distillater	GFL – Germany
Micropipettes (0.5-5,100-1000)µl	Huawei and dragon med- Germany
Refrigerator double door model SR32EMB	Cool tech /Korea

Table (3-3): Disposable used during this study

Item	Manufacturer
Aerosol Resistant Micropipette tips (10µl)	**Bio-Basic / Canada**

Aerosol Resistant Micropipette tips (100-200µl)	**Promega / USA**
Aerosol Resistant Micropipette tips (10-100µl)	**Bio-Basic / Canada**
Aerosol Resistant Micropipette tips(1000µl)	**Promega / USA**
Disposable cups 10ml	**Shanghai Orsia Medical Technology /chine**
Eppendorf tube (1.5ml)	**China**
Gel tubes 5 ml	**Shanghai Orsia Medical Technology /chine**
Gloves	**Bio Basic/China**
Medical cotton	**Kardelen / Turkey**
Syringe 3,5,10 ml	**TG / Malaysia**

3.2 Patients and control groups

This study was done on a group of prisoners in the Najaf police prison (Najaf governorate), who were drug users, for period from June to August 2021. This study included 40 persons who abuse taken, 15 persons were not abuse apparently, the group was selected as a control group. The ages of persons and control group ranged between (18-25) years.

3.2.1 Blood Samples

Five venous bloods collected from each sample of the study, samples ware place in tubes containing a gel, the blood was separated by centrifuge at 3000 rpm for 15 minutes, and the remaining serum was distributed to Eppendorf tube and then stored in a deep freeze at -20C° until .

3.2.2 Urine Samples

Five to ten milliliters urine collected from each sample of the study, samples ware place in disposable cups, and distributed to rapid test panel (urine) .

3.2.3 Drug Test Principle

The One Step Drug Screen Test Card is an immunoassay based on the principle of competitive binding. Drugs that may be present in the urine specimen compete against their respective drug conjugate for binding sites on their specific antibody.

During testing, a urine specimen migrates upward by capillary action. A drug, if present in the urine specimen below its cutoff concentration, will not saturate the binding sites of its specific antibody. The antibody will then react with the drug-protein conjugate and a visible colored line will appear in the test line region (T) of the specific drug strip.

The presence of drug above the cutoff concentration will saturate all the binding sites of the antibody. Therefore, the colored line will not form in the test line region (T).A drug-positive urine specimen will not generate a colored line in the specific test line region (T) of the strip because of drug competition, while a drug-negative urine specimen or a specimen containing a drug concentration lower than the cutoff will generate a line in the test line region (T) because of the absence of drug competition. To serve as a procedural control, a colored line will always appear at the control line region (C), indicating that proper volume of specimen has been added and membrane wicking has occurred.

3.3 Experimental design

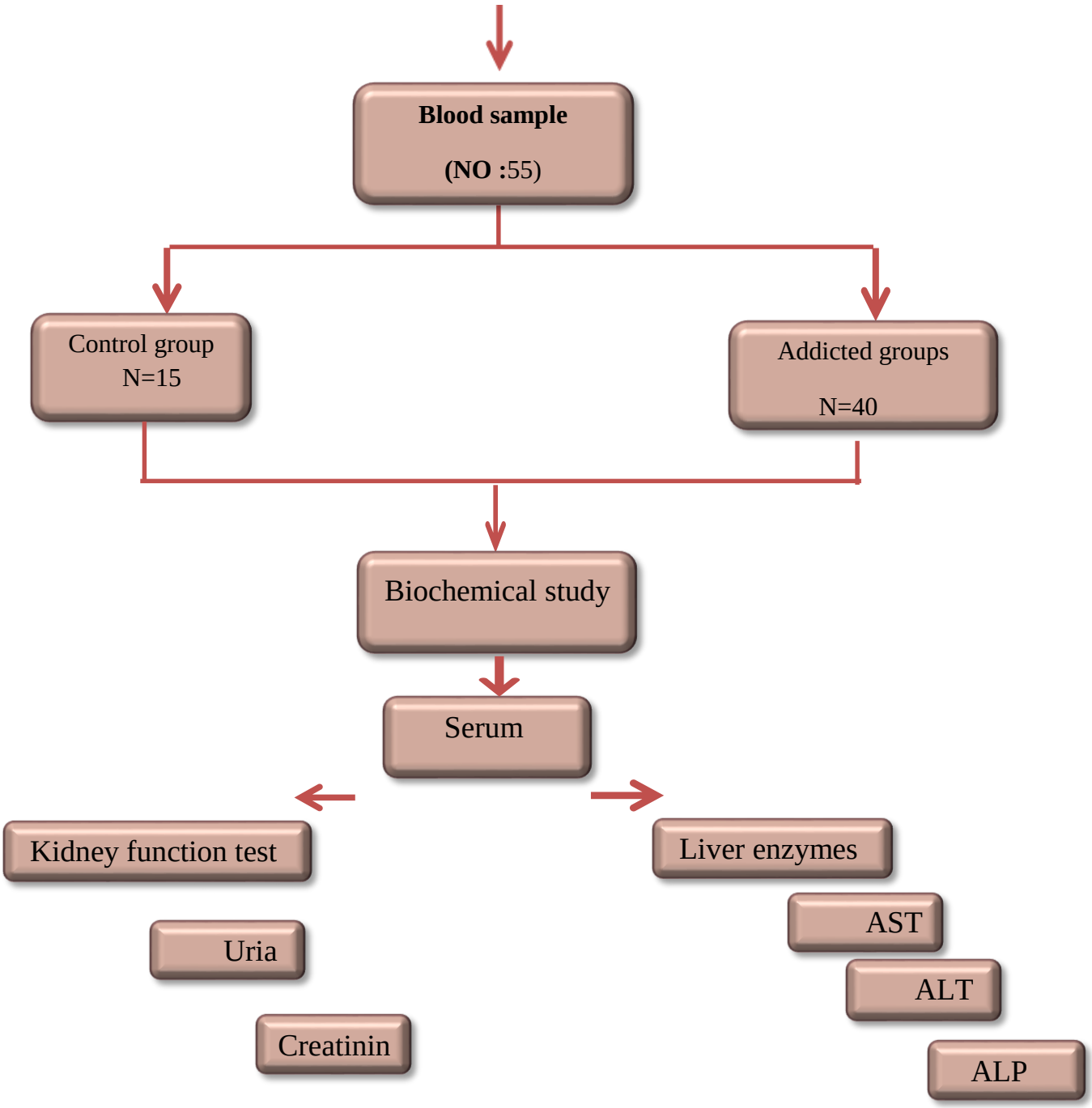

Figure (3-1) study design

3.4. Biochemical Study

3.4.1 Liver Enzyme AST, ALT and ALP

3.4.1.1 AST and ALT test reagent preparation

Serum Aspartate aminotransferase AST and Alanine aminotransferase ALT activities were determined by using the Bio diagnostic's Enzymatic Colorimetric kits and spectrophotometers at 340 nm wave length
according to the following procedure:

1- 1000 µl of working reagent was added to the tube

2- 100 µl of sample was added to the tube.

3- the tube mixed and incubated at 37C° for 1 minute. the change in absorbance per minute (OD / min) was measured during 3 minutes.

Calculation
SGPT or SGOT conc. (U/L) = (OD / min) x 1745

3.4.1.2 Alkaline phosphatase (ALP)

Alkaline phosphatase estimated by using spectrophotometers at 510 nm wave length according to the following procedure:

The tubes prepared as follows: reagent blank, specimen blank, standard, and assay;

Table (3-4) kit procured of ALP enzyme

	Reagent Blank	**Specimen blank**	**Standard**	**Assay**
Reagent R1	2 ml	2 ml	2 ml	2ml
Incubate 5 minute at 37 °c .				
Specimen	-	-	-	50 ML
Reagent R2	-	-	50 ML	-
Let stand exactly 15 minutes at 37°c .				
Reagent R3	0.5 ml	0.5 ml	0.5 ml	0.5 ml
Mix well, incubate to bring to temperature and read initial absorbance (A1) Then add:				
Reagent R4	0.5 ml	0.5 ml	0.5 ml	0.5 ml
Specimen	-	50 ml	-	-
demineralized water	50 ml	-	-	-
Mix . Incubate 10 minute at room temperature and away from light . Read absorbtion of the blank specimen and assay at 510 nm against reagent blank .				

Calculation

Calculate the result as follows:

$$\text{ALP activity (Kind and king unit /100 ml)} = \frac{\text{Abs Assay - Abs Specimen blank}}{\text{Abs Standard}} \times 20$$

3.4.2 kidney function test

3.4.2.1 creatinine

This procedure is based upon a modification of the original picrate reaction (Jaffe), Creatinine under alkaline conditions reacts with picrate ions forming a reddish complex. The formation rate of the complex measured through the increase of absorbance in a prefixed interval of time is proportional to the concentration of creatinine in the sample.

$$\text{Creatinine + Picric acid} \xrightarrow[37^{o}C]{pH > 12} \text{Red addition complex}$$

REAGENT COMPOSITION

R1 Picric acid. Picric acid 25 mmol/L

R2 Alkaline buffer. Phosphate buffer 300 mmol/L pH 12.7, SDS 2.0 g/L (w/v). Xi R:36/37/38

CAL Creatinine standard. Creatinine 2 mg/dL (177 µmol/L). Organic matrix based primary standard. Concentration value is traceable to Standard Reference Material 914a.

Reagent Preparation

Working reagent. Mix 1 volume of R1 + 1 volume of R2. Stable for 1 week at room temperature, stored tightly closed and protected from light

Sample Preparation

Creatinine in serum or plasma is stable up to 24 hours at 2-8ºC. Freeze for longer storage.

PROCEDURE

1- Preincubate working reagent, samples and standard to reaction temperature (37ºC).
2- Set the photometer to 0 absorbance with distilled water.
3- Pipette into a cuvette:

Working reagent	1.0 ml
Sample	100m ml

4- Mix gently. Insert cuvette into the temperature-controlled instrument and start stopwatch.
5- Record absorbance at 510 nm after 30 seconds (A1) and after 90 seconds (A2) of the sample or standard addition.

Calculation

$$\frac{(A_2 - A_1)\ \text{Sample}}{(A_2 - A_1)\ \text{Standard}} \times C\ \text{Standard} = \text{mg/dL creatinine}$$

3.4.2.2 Urea

Urea - Kit S enables end point enzymatic determination of urea concentrations (Urease - modified Berthelot reaction) in human urine. serum or plasma. Urease hydrolyzes urea by producing ammonium:

$$\text{Urea} + H_2O \xrightarrow{\text{urease}} 2\,NH_3 + CO_2$$

In an alkaline medium, the ammonium ions react with the salicylate and hypochlorite to form green colored indophenol (2,2 dicarboxylindophenol). The reaction is catalyzed by sodium nitroprusside.

$$NH_4^{*} + \text{salicylate} + \text{hypochlorite} \longrightarrow \text{indophenol}$$

The color intensity is proportional to the urea concentration in the sample. The absorbance was read at 580 nm wave length (According to biomérieux company) .

Reagent	**blank**	**Standard**	**Sample**
Standard Sample Working solution	- - 1m l	10 ml - 1 ml	- 10 ml 1 ml
the reagent were mix and incubated for 5 minute at 20 -25° C			
Reagent 4	200 *ml*	200 *ml*	200 *ml*
The reagent were mixed and incubated for 10 minutes at 20- 25° C			

Color intensity was stable in the dark for 2 hours at 20 -25° C

Calculation

$$\text{Sample concentration} = \frac{\text{A sample}}{\text{A standard}} * \text{Concentration of standard (8.33mmol)}$$

Chapter Four

Results and Discussion

4. Results and Discussion

4.1 Multi Drug rapid test in urine

Chromatography is one of the fastest and most common tests, so drug discovery and some drugs are used as one of the most common methods in emergencies and workplaces for accuracy and speed. This test is based on the ratio of soluble substances in urine, where adolescents and young people are screened even knowing the type of narcotic drug and prescription medication in case of emergency. The best ways to use them in identifying unknown substances. Alcohol and drugs vary substantially in their windows of detection, largely owing to their degree of fat solubility. For example, THC and other highly fat-soluble compounds have a very long half-life of elimination and can be detected in urine up to weeks after last use among heavy users' levels may vary with urine concentration, the amount of drug used, and time since last use. Additionally, because highly sensitive drug testing may detect substances at limits far lower than therapeutic doses (Hadland and Levy,2016).

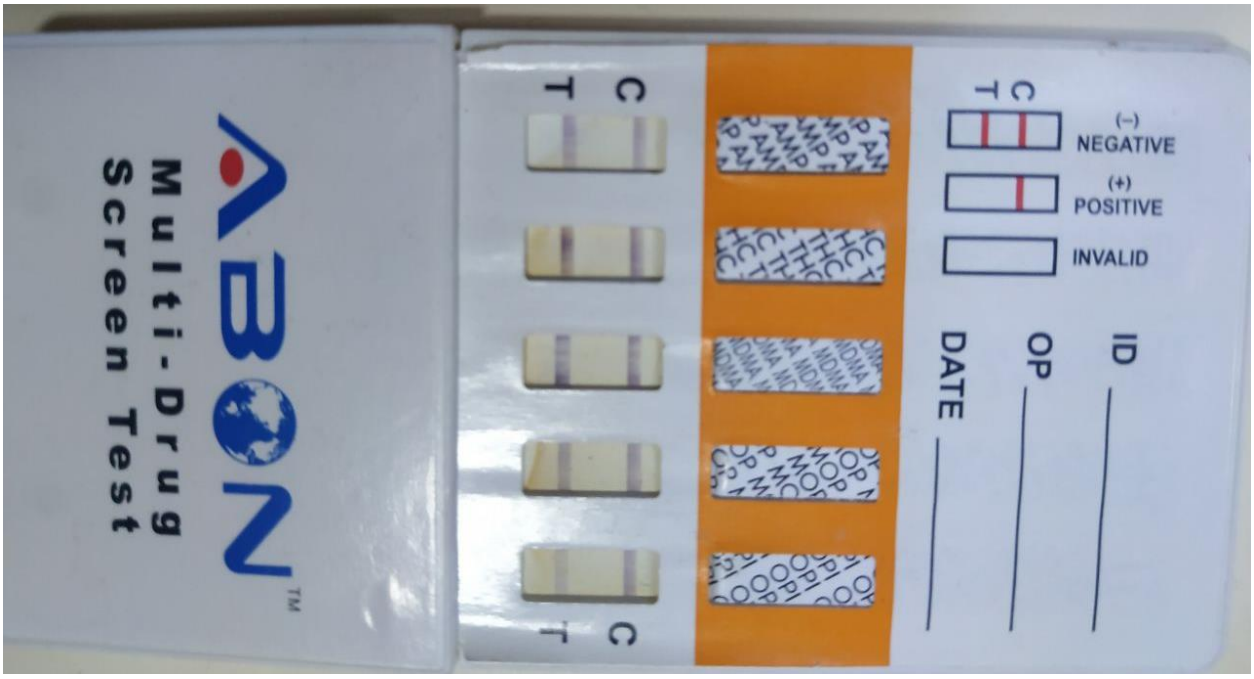

Figure (4-1) Multi drug test panel for urine

4.2. Result of biochemical study

4.2.1 Effect of drugs on liver enzymes

The current study includes forty sample of abuse and fifteen sample as control group, the aimed of this study to use forensic to detect the effect of abuse Marijuana (THC) and amphetamine (AMP) on function of liver and kidney. AST enzyme was estimated in serum of patient and control study, and the result showed elevated in AST level in sample than control group, and there is a significate differences as showed in Table (4-1).

Table (4-1) AST conc. in serum of sample and control group

AST	Control	Addicts	*P-value*
Range	15-33	10.5-90.9	0.003*
Median	27	34.65	
Mean+ Std. Error	26.133±1.376	44.952 ±3.674	

P ≤0.005

The clinical implications of marijuana use are diverse, and potentially both harmful and beneficial, the health risks of marijuana use are well documented: including liver disorder, kidney failure, dose-dependent respiratory symptoms such as shortness of breath, coughing and increased sputum production (Patkar *et al.*,2005; Tanimowo and Onaolapo, 2007). Long-term marijuana abuse is associated with cognitive deficits, as well as with cerebrovascular disorders such as stroke (Jayanthi *et al*., 2010).

Interestingly, end cannabinoids, endogenous cannabinoids that bind to the same CB1 and CB2 receptors as tetrahydrocannabinol (THC), the active component in marijuana, are highly up regulated in chronic liver disease and may contribute to the pathogenesis of various liver diseases (Eccleston and Lucey, 2017).

ALT enzyme was estimated in serum of sample and control study, and the result showed elevated in ALT level in sample than control group, and there is a significant differences as showed in Table (4-2).

Table (4-2) ALT level in serum of sample and control group

ALT	Control	Patients	*P*
Range	15-50	5.8-120.3	0.047*
Median	35	42.9	
Mean ± Std. Error	34.4 ± 2.332	52.717 ±5.414	

P≤0.005

The results of the study showed a significant increase (P≤0.05) in the group of abuse when compared to the control group (AST & ALT) in enzyme activity , there is a significant increase in AST enzyme activity (44.952) when compare to control group (26.133),table (4-1), While ALT enzyme activity was also a significant increase (0.04), higher ALT level in serum of sample group (52.717) when compares to control group (34.4),and the resulting accumulation of chemical compounds in the liver, The result is in agreement with the study conducted by Di *Marzo et al.,2009* which confirmed the presence of an increase in the effectiveness of groups exposed to chemical compounds at (AST) enzyme compared to the control group.

Table (4-3) ALP level in serum of sample and control group

ALP	Control	Patients	*P*
Range	53-157	90-194	0.001*
Median	100	134.5	
Mean ± Std. Error	107.8 ± 9.83	140.323 ± 3.971	

P≤0.005

The results of the study showed a significant (P≤0.001*) increase in the effectiveness of the alkaline phosphatase enzyme in the patients (140.323) when compared with the control group (107.8). The increase may be due to the effect of enzyme activity by the oxides released by the chemicals involved in the composition of those pills, especially if we know It is a way of changing the way Captagon is manufactured by adding other substances to it to produce (Counterfeit Captacone is cheaper, it is called counterfeit Captagon, it adds more health problems, and from the substances that are added Captagon) to the counterfeit Captagon: Caffeine, amphetamine, quinine, theophylline and other substances that cause liver damage [ephedrine](Baer, 2004) ,and a group of patients (ALP) indicated that there is an increase in the enzyme] who abuse sedative drugs excessively (Nesif and Mushtaq,2010).

This study also agreement with other study that shows higher scores in Aspartate amino transferase level and also elevated in Alanine amino transferase level (SGPT) cannabis abusers showed higher scores in relation with control group, the elevated of these enzymes are to be the more insightful determine for evaluating hepatocellular damage (Copeland and Swift, 2009).

Other study linked Cannabis smoking and liver function and showed that adult addicted men smoked Cannabis for different periods showed slight numerical

increase in (ALP) activity with the increase of the length of the period of Cannabis smoking. In contrast the activity of the (ALT) and the (AST) reported significantly lower levels compared to the nonsmokers' group (Brunet *et al.*,2013)

Several studies have discussed of Marijuana and suggests that the Marijuana could exacerbate liver disease (Caraceni *et al*.,2008). In contrast to the potential deleterious effects of marijuana, it may provide some therapeutic effects for patients with liver disease. Marijuana use has been shown to positively affect various neurological and psychological phenomena such as mood, appetite, analgesia and nausea control (Gabbay *et al*.,2005). In addition, cannabinoids have been shown to possess immunomodulatory and anti-inflammatory properties in peripheral tissues via CB2 receptor activation, potentially reducing the risk of rejection (Larson and Curtis, 2006).

4.2.2 Effect of drugs on kidney function

The result of study, as showed in Table (4-4), indicates there is a non-significant increase (P>0.05) in the serum urea rate of the group of drug users slightly increase (28.273) when compared to the control group (26.533) , this result disagreement with studies conducted by Pantelias, and Grapsa, (2011) ,that found increase in urea in serum od abuse than in control group and explain that this increase may be caused by damage to the collecting tubules due to the kidneys suffering from depositions of chemicals released by those drugs, which as a result, it leads to a decrease in the efficiency of the kidneys in filtering blood urea (Rahman *et al*

.,2009) .which was indicated by 22] In his study of the effect of the use of cortisone on the permeability or osmosis of kidney tissues, which leads to a decrease in the efficiency of the kidneys in filtering uric acid, which causes an increase in the percentage of its presence in the blood (Kazory, and Aiyer, 2013).

Table (4-4) Urea level in serum of sample and control group

Urea	Control	Patients	*P*
Range	15-41	14.9-52.2	0.432
Median	25	28.35	
Mean ± Std. Error	26.533 ± 1.743	28.273 ± 1.173	

P >0.005

The result of measurement of creatinine level showed a non-significant increase (P>0.408 mg/dl) in the blood serum creatinine of the in-abuse group (0.814) and (0.76) in the serum of the control sample (Table 4-5), and this reset disagreement with studies conducted by Mazzeo and Raiola, (2018) that explain that the reason of increase creatinine level may be explained by high blood urea causes damage to body tissues as they are primary toxins, which causes an increase in the excretion of creatinine in the kidneys, which affects the work of the kidneys and its efficiency in excreting ,Creatinine and this raises its level in the blood serum, as indicated that the high level of urea in the blood causes a noticeable rise in serum creatinine due to the mechanical and chemical damage caused by urea in body tissues such as the brain and liver (Bartoli *et al*.,2016).

Table (4-5) Creatinine level in serum of sample and control group

Creatinine	Control	Patients	*P*
Range	0.3-1.2	0.19-1.3	0.408
Median	0.8	0.82	
Mean ± Std. Error	0.76 ± 0.058	0.814 ±0.033	

P >0.005

Accompanying health impacts of AMPs will become more common when used excessively of young people with elicit use of these drugs. Induced adverse effects of AMPs including mortality, particularly in young patients with serious, hypertension, hyperthermia or hyponatremia are discussable. The deadly side effects of AMPs should be considered in the clinic. One of the more important complications of the AMPs is associated with their renal defects due to rhabdomyolysis, necrotizing renal maculopathy and malign hypertension. Therefore, nephropathy after AMPs (Mokhtari *et al*.,2018).

Conclusions

and

Recommendation

Conclusions;

1. Abuse of THC and AMP caused significant elevated in liver enzyme GOT, GPT and ALT
2. Abuse of THC and AMP caused non-significant elevated in creatinine and urea.

Recommendations:

1-Using rapid test as routine work in Police stations .

2- Studying immunological parameters on effect of abuse substance.

3- Studying the effect of adduct on the antioxidant enzymes.

References

References;

Alhamad, T., Koraishy, F. M., Lam, N. N., Katari, S., Naik, A. S., Schnitzler, M. A., ... and Lentine, K. L. (2019). Cannabis dependence or abuse in kidney transplantation: implications for posttransplant outcomes. Transplantation, 103(11), 2373.

Al-Hemiary, N., and Talib, M. (2010). Substance Abuse and Dependence: In the Records of the Iraqi Hospitals and Health Centers During the Year 2008. IRAQI POSTGRADUATE MEDICAL JOURNAL, 9(2).

Al-khafaji, A. M. (2010). Substance dependence in Diwania province. Kufa Med J, 13, 118-128.

Almeida, S. P. D., and Silva, M. T. A. (2003). Ecstasy (MDMA): effects and patterns of use reported by users in Sao Paulo. Brazilian Journal of Psychiatry, 25(1), 11-17.

Anderson, A. H., Yang, W., Hsu, C. Y., Joffe, M. M., Leonard, M. B., Xie, D., ... and CRIC Study Investigators. (2012). Estimating GFR among participants in the Chronic Renal Insufficiency Cohort (CRIC) study. American journal of kidney diseases, 60(2), 250-261.

Arneson, W., and Brickell, J. (2007). Assessment of liver function. *Clinical Chemistry: A Laboratory Perspective*, 233-266.

Baer, D. M. (2004). Cut-off and toxicity levels for drugs-of-abuse testing. MLO: medical laboratory observer, 36(13 Suppl), 10-11.

Bartoli, E. (2016). Adverse effects of drugs on the kidney. *European journal of internal medicine*, *28*, 1-8.

References

Bishop, G. A., and McCaughan, G. W. (2001). Immune activation is required for the induction of liver allograft tolerance: implications for immunosuppressive therapy. *Liver Transplantation*, *7*(3), 161-172.

Blickman, T. (2011). Amphetamine type stimulants and harm reduction. Amsterdam, Netherlands: Transnational Institute (TNI).

Bonomi, A. E., Anderson, M. L., Rivara, F. P., and Thompson, R. S. (2007). Health outcomes in women with physical and sexual intimate partner violence exposure. Journal of Women's Health, 16(7), 987-997.

Brunet, L., Moodie, E. E., Rollet, K., Cooper, C., Walmsley, S., Potter, M., ... & Canadian Co-infection Cohort Investigators. (2013). Marijuana smoking does not accelerate progression of liver disease in HIV–hepatitis C coinfection: a longitudinal cohort analysis. Clinical Infectious Diseases, 57(5), 663-670.

Burtis, C. A., and Bruns, D. E. (2014). *Tietz fundamentals of clinical chemistry and molecular diagnostics-e-book*. Elsevier Health Sciences.

Caraceni, P., Domenicali, M., and Bernardi, M. (2008). The endocannabinoid system and liver diseases. Journal of neuroendocrinology, 20, 47-52.

Clarke, T. K., Weiss, A. R., Ferarro, T. N., Kampman, K. M., Dackis, C. A., Pettinati, H. M., ... and Berrettini, W. H. (2014). The dopamine receptor D2 (DRD2) SNP rs1076560 is associated with opioid addiction. Annals of human genetics, 78(1), 33-39.

Cone, E. J. (1995). Pharmacokinetics and pharmacodynamics of cocaine. Journal of analytical toxicology, 19(6), 459-478.

Copeland, J., and Swift, W. (2009). Cannabis use disorder: epidemiology and management. International Review of Psychiatry, 21(2), 96-103.

References

Crowe, A. V., Howse, M., Bell, G. M., and Henry, J. A. (2000). Substance abuse and the kidney. Qjm, 93(3), 147-152.

Csete, J., Kamarulzaman, A., Kazatchkine, M., Altice, F., Balicki, M., & Buxton, J. and Beyrer, C.(2016). Public health and international drug policy. Lancet, 387(10026), 1427-1480.

De Letter, E. A., Piette, M. H., Lambert, W. E., andCordonnier, J. A. (2006). Amphetamines as potential inducers of fatalities: a review in the district of Ghent from 1976-2004. Medicine, science and the law, 46(1), 37-65.

Degenhardt, L., Hall, W., and Lynskey, M. (2001). The relationship between cannabis uses and other substance use in the general population. Drug and alcohol dependence, 64(3), 319-327.

Di Marzo, V., Cote, M., Matias, I., Lemieux, I., Arsenault, B. J., Cartier, A., ... and Després, J. P. (2009). Changes in plasma endocannabinoid levels in viscerally obese men following a 1year lifestyle modification programme and waist circumference reduction: associations with changes in metabolic risk factors. Diabetologia, 52(2), 213-217.

Donnelly, M., Rapoport, J. L., Potter, W. Z., Oliver, J., Keysor, C. S., and Murphy, D. L. (1989). Fenfluramine and dextroamphetamine treatment of childhood hyperactivity: Clinical and biochemical findings. Archives of general psychiatry, 46(3), 205-212.

Easton, N., Steward, C., Marshall, F., Fone, K., and Marsden, C. (2007). Effects of amphetamine isomers, methylphenidate and atomoxetine on synaptosomal and synaptic vesicle accumulation and release of dopamine and noradrenaline in vitro in the rat brain. Neuropharmacology, 52(2), 405-414.

References

Eccleston, J. L., and Lucey, M. R. (2017). Substance use disorders before and after liver transplantation. Clinical liver disease, 10(4), 100.

Faraone, S. V., Biederman, J., Morley, C. P., and Spencer, T. J. (2008). Effect of stimulants on height and weight: a review of the literature. Journal of the American Academy of Child & Adolescent Psychiatry, 47(9), 994-1009.

Fernández, M. D. M. R., Di Fazio, V., Wille, S. M., Kummer, N., & Samyn, N. (2014). A quantitative, selective and fast ultra-high performance liquid chromatography tandem mass spectrometry method for the simultaneous analysis of 33 basic drugs in hair (amphetamines, cocaine, opiates, opioids and metabolites). Journal of Chromatography B, 965, 7-18.

Friedman, H., Pross, S., and Klein, T. W. (2006). Addictive drugs and their relationship with infectious deseases. FEMS Immunology & Medical Microbiology, 47(3), 330-342.

Gabbay, E., Avraham, Y., Ilan, Y., Israeli, E., and Berry, E. M. (2005). Endocannabinoids and liver disease–review. Liver International, 25(5), 921-926.

Gray, K. M., Carpenter, M. J., Baker, N. L., DeSantis, S. M., Kryway, E., Hartwell, K. J., ... and Brady, K. T. (2012). A double-blind randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents. American Journal of Psychiatry, 169(8), 805-812.

Greene, S. L., Dargan, P. I., O'connor, N., Jones, A. L., and Kerins, M. (2003). Multiple toxicity from 3, 4-methylenedioxymethamphetamine ("ecstasy"). The American journal of emergency medicine, 21(2), 121-124.

Hadland, S. E., and Levy, S. (2016). Objective testing–urine and other drug tests. *Child and adolescent psychiatric clinics of North America*, *25*(3), 549.

References

Håkansson, A., and Jesionowska, V. (2018). Associations between substance use and type of crime in prisoners with substance use problems–a focus on violence and fatal violence. Substance abuse and rehabilitation, 9, 1.

Harris, E. H. (2005). Elevated liver function tests in type 2 diabetes. *Clinical diabetes*, *23*(3), 115-119.

Heal, D. J., Cheetham, S. C., Prow, M. R., Martin, K. F., and Buckett, W. R. (1998). A comparison of the effects on central 5-HT function of sibutramine hydrochloride and other weight-modifying agents. British journal of pharmacology, 125(2), 301-308.

Heal, D. J., Smith, S. L., Gosden, J., and Nutt, D. J. (2013). Amphetamine, past and present–a pharmacological and clinical perspective. Journal of psychopharmacology, 27(6), 479-496.

Ho, C., Martinusen, D., and Lo, C. (2019). A review of cannabis in chronic kidney disease symptom management. Canadian journal of kidney health and disease, 6, 2054358119828391.

Jackson, A. R. W., and Jackson, J. M. (2008). The examination of body fluids. Jackson ARW, Jackson JM, Forensic Science, Pearson Prentice Hall, Harlow, England.

Jackson, G. E. (2009). Drug-Induced Dementia: a perfect crime. Bloomington, IN: AuthorHouse.

Jayanth, S. H., Hugar, B. S., Praveen, S., and Girish Chandra, Y. P. (2017). Glue sniffing. Medico-Legal Journal, 85(1), 38-42.

References

Jayanthi, S., Buie, S., Moore, S., Herning, R. I., Better, W., Wilson, N. M., ... and Cadet, J. L. (2010). Heavy marijuana users show increased serum apolipoprotein C-III levels: evidence from proteomic analyses. Molecular psychiatry, 15(1), 101-112.

Kazory, A., and Aiyer, R. (2013). Synthetic marijuana and acute kidney injury: an unforeseen association. Clinical kidney journal, 6(3), 330-333.

Kendler, K. S., Ohlsson, H., Sundquist, K., and Sundquist, J. (2014). Peer deviance, parental divorce, and genetic risk in the prediction of drug abuse in a nationwide Swedish sample: evidence of environment-environment and gene-environment interaction. JAMA psychiatry, 71(4), 439-445.

Kiyatkin, E. A. (2014). State-dependent and environmental modulation of brain hyperthermic effects of psychoactive drugs of abuse. Temperature, 1(3), 201-213.

Kuczenski, R., Segal, D. S., Cho, A. K., and Melega, W. (1995). Hippocampus norepinephrine, caudate dopamine and serotonin, and behavioral responses to the stereoisomers of amphetamine and methamphetamine. Journal of Neuroscience, 15(2), 1308-1317.

Kunis, C. L., Aggarwal, N., and Appel, G. B. (2008). Illicit drug abuse and renal disease. Clinical Nephrotoxins, 595-616.

Lai, G. Y., Weinstein, S. J., Albanes, D., Taylor, P. R., McGlynn, K. A., Virtamo, J., ... and Freedman, N. D. (2013). The association of coffee intake with liver cancer incidence and chronic liver disease mortality in male smokers. *British journal of cancer*, *109*(5), 1344-1351.

References

Larson, A. M., and Curtis, J. R. (2006). Integrating palliative care for liver transplant candidates:"too well for transplant, too sick for life". JAMA, 295(18), 2168-2176.

Laterza, O. F., Price, C. P., and Scott, M. G. (2002). Cystatin C: an improved estimator of glomerular filtration rate?. *Clinical chemistry*, *48*(5), 699-707.

LeBeau, M. A. (2008, April). Guidance for improved detection of drugs used to facilitate crimes. In Therapeutic drug monitoring (Vol. 30, No. 2, pp. 229-233). LWW.

Legg, K. M., Powell, R., Reisdorph, N., Reisdorph, R., and Danielson, P. B. (2017). Verification of protein biomarker specificity for the identification of biological stains by quadrupole time-of-flight mass spectrometry. Electrophoresis, 38(6), 833-845.

Li, R., Norman, S., and Schober, J. (2015). Forensic biology. CRC Press.

Lotfi, P. M., Javadimehr, M., and Adrome, M. (2015). Attitudes of students living in dormitories of Zahedan University of medical sciences towards the causes of drug addiction. International journal of high-risk behaviors & addiction, 4(2).

Manetti, L., Cavagnini, F., Martino, E., and Ambrogio, A. (2014). Effects of cocaine on the hypothalamic–pituitary–adrenal axis. Journal of endocrinological investigation, 37(8), 701-708.

Manetti, L., Cavagnini, F., Martino, E., and Ambrogio, A. (2014). Effects of cocaine on the hypothalamic–pituitary–adrenal axis. Journal of endocrinological investigation, 37(8), 701-708.

Mazzeo, F., and Raiola, G. (2018). An investigation of drugs abuse in sport performance.

References

Mills, K. T., Xu, Y., Zhang, W., Bundy, J. D., Chen, C. S., Kelly, T. N., ... and He, J. (2015). A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. Kidney international, 88(5), 950-957.

Mitchell, A. L. (2006). Medical Consequences of Cocaine. Journal of Addictions Nursing, 17(4), 249-249.

Mokhtari, T., Sheikhazadi, A., Hassanzadeh, G., Safari, M., Sheikhbahaei, F., Faghir-Ghanesefat, H., and Rezaei, M. (2018). Potential adverse effects of amphetamines on kidney; a narrative review on current knowledge. Journal of Renal Injury Prevention, 7(4), 218-223.

Muro, C. K., and Lednev, I. K. (2017). Identification of individual red blood cells by Raman micro spectroscopy for forensic purposes: in search of a limit of detection. Analytical and bioanalytical chemistry, 409(1), 287-293.

Nesif, A. H., and Mushtaq, T. (2010). Substance abuse and dependence: in the records of the Iraqi hospitals and health centers during the year 2008.

Nolan, S., Walley, A. Y., Heeren, T. C., Patts, G. J., Ventura, A. S., Sullivan, M. M., ... and Saitz, R. (2017). HIV-infected individuals who use alcohol and other drugs, and virologic suppression. AIDS care, 29(9), 1129-1136.

Norris, K. C., Thornhill-Joynes, M., Robinson, C., Strickland, T., Alperson, B. L., Witana, S. C., & Ward, H. J. (2001). Cocaine use, hypertension, and end-stage renal disease. American journal of kidney diseases, 38(3), 523-528.

Nymoen Aasbrenn, M., Skeie, I., and Berild, D. (2019). Compliance to antibiotic guidelines leads to more appropriate use of antibiotics in skin and soft tissue infections in injecting drug users. Infectious Diseases, 51(8), 570-577.

References

Obot, I. S., and Room, R. (2005). Alcohol, gender and drinking problems: perspectives from low- and middle-income countries. World Health Organization.

Orriols, L., Salmi, L. R., Philip, P., Moore, N., Delorme, B., Castot, A., and Lagarde, E. (2009). The impact of medicinal drugs on traffic safety: a systematic review of epidemiological studies. Pharmacoepidemiology and drug safety, 18(8), 647-658.

Orth, S. R., and Hallan, S. I. (2008). Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients—absence of evidence or evidence of absence?. Clinical Journal of the American Society of Nephrology, 3(1), 226-236.

Oye, G. (2007). Alcohol, Gender and Drinking Problems: Perspectives from Low- and Middle-Income Countries. Edited by Obot, Isidore S. & Room, Robin. World Health Organization. 2005. 235 pp. US $45.00 (pb). ISBN 9241593504. The British Journal of Psychiatry, 190(3), 277-277.

Pantelias, K., and Grapsa, E. (2011). Drug abuse and kidney. Hippokratia, 15(2), 4-8.

Pasala, S., Barr, T., and Messaoudi, I. (2015). Impact of alcohol abuse on the adaptive immune system. Alcohol research: current reviews, 37(2), 185.

Patkar, A. A., Patkar, A. A., Batra, V., Mannelli, P., Evers-Casey, S., Vergare, M. J., and Leone, F. T. (2005). Medical symptoms associated with tobacco smoking with and without marijuana abuse among crack cocaine-dependent patients. American Journal on Addictions, 14(1), 43-53.

References

Petit, A., Karila, L., Chalmin, F., and Lejoyeux, M. (2012). Methamphetamine addiction: a review of the literature. Journal of Addiction Research & Therapy S, 1, 1-6.

Pouget, E. R., Sandoval, M., Nikolopoulos, G. K., and Friedman, S. R. (2015). Immediate impact of Hurricane Sandy on people who inject drugs in New York City. Substance use & misuse, 50(7), 878-884.

Pourallahvirdi, M., Rahmani, F., Ranjbar, F., Ebrahimi Bakhtavar, H., & Ettehadi, A. (2016). Major causes of drug abuse from the viewpoint of addicted persons referred to addiction treatment centers of Tabriz City, Iran. Archives of Neuroscience, 3(3).

Price, C. P., and Finney, H. (2000). Developments in the assessment of glomerular filtration rate. *Clinica chimica acta*, *297*(1-2), 55-66.

Rafaiee, R., Olyaee, S., and Sargolzaiee, A. (2013). The relationship between the type of crime and drugs in addicted prisoners in Zahedan Central Prison. International journal of high-risk behaviors & addiction, 2(3), 139.

Rafaiee, R., Olyaee, S., and Sargolzaiee, A. (2013). The relationship between the type of crime and drugs in addicted prisoners in Zahedan Central Prison. International journal of high-risk behaviors & addiction, 2(3), 139.

Rahman, M. K., Rahman, F., Rahman, T., and Kato, T. (2009). Dopamine-β-hydroxylase (DBH), its cofactors and other biochemical parameters in the serum of neurological patients in Bangladesh. International journal of biomedical science: IJBS, 5(4), 395.

References

Rai, H. S., and Winder, G. S. (2017). Marijuana use and organ transplantation: a review and implications for clinical practice. Current psychiatry reports, 19(11), 1-11.

Ramachandran, R., and Kakar, S. (2009). Histological patterns in drug-induced liver disease. Journal of clinical pathology, 62(6), 481-492.

Ravera, S., van Rein, N., De Gier, J. J., and de Jong-van den Berg, L. T. (2011). Road traffic accidents and psychotropic medication use in the Netherlands: a case–control study. British journal of clinical pharmacology, 72(3), 505-513.

Resnick, H. S., Walsh, K., Schumacher, J. A., Kilpatrick, D. G., and Acierno, R. (2013). Prior substance abuse and related treatment history reported by recent victims of sexual assault. Addictive Behaviors, 38(4), 2074-2079.

Salazar, J. H. (2014). Overview of urea and creatinine. *Laboratory medicine*, *45*(1), e19-e20.

Salo, R., Flower, K., Kielstein, A., Leamon, M. H., Nordahl, T. E., and Galloway, G. P. (2011). Psychiatric comorbidity in methamphetamine dependence. *Psychiatry research*, *186*(2-3), 356-361.

Stark, A. L., Hickson, L. J., Larrabee, B. R., Thusius, N. J., Karpyak, V. M., Hall-Flavin, D. K., and Schneekloth, T. D. (2019). Cannabis abuse and dependence in kidney transplant candidates. Journal of psychosomatic research, 121, 68-73.

Sarkar, D., Jung, M. K., and Wang, H. J. (2015). Alcohol and the immune system. Alcohol research: current reviews, 37(2), 153.

Singh, D., Tripathi, M., Karki, P., and Bhandari, S. (2009). Glue Sniffing Among Street Children in Gaushala and Sundhara Area of Kathmandu Valley.

Sinha, A., Lewis, O., Kumar, R., Yeruva, S. L. H., and Curry, B. H. (2016). Amphetamine abuse related acute myocardial infarction. Case reports in cardiology, 2016.

Tanimowo, M. O., and Onaolapo, Y. A. (2007). The pattern of tobacco use among non-pulmonary tuberculosis patients attending a chest clinic in South-Western Nigeria. Nigerian journal of clinical practice, 10(4), 314-318.

Tao, R., Fray, A., Aspley, S., Brammer, R., Heal, D., and Auerbach, S. (2002). Effects on serotonin in rat hypothalamus of D-fenfluramine, aminorex, phentermine and fluoxetine. European journal of pharmacology, 445(1-2), 69-81.

Tulsidas, H. (2010). Glue sniffing: A review. Proceedings of Singapore Healthcare, 19(4), 312-318.

Uddin, M. S., Sufian, M. A., Kabir, M. T., Hossain, M. F., Nasrullah, M., Islam, I., ... and Khanum, S. (2017). Amphetamines: Potent recreational drug of abuse. J Addict Res Ther, 8(4), 1-12.

Uddin, M. S., Sufian, M. A., Kabir, M. T., Hossain, M. F., Nasrullah, M., Islam, I., ... and Khanum, S. (2017). Amphetamines: Potent recreational drug of abuse. J Addict Res Ther, 8(4), 1-12.

Wells, D. L., and Ott, C. A. (2011). The "new" marijuana. Annals of Pharmacotherapy, 45(3), 414-417.

Yang, C. Y., Ho, M. C., Jeng, Y. M., Hu, R. H., Wu, Y. M., and Lee, P. H. (2007). Management of hepatic angiomyolipoma. *Journal of Gastrointestinal Surgery*, *11*(4), 452-457.

Zhang, L., Zhang, S., Sun, M., Li, H., Li, Y., Fu, Z., ... and Lin, L. (2017). Noncontact discrimination of animal and human blood with vacuum blood vessel

and factors affects the discrimination. Infrared Physics & Technology, 81, 210-214.

الخلاصة:

اجريت هذه الدراسة لمعرفة تأثير الادمان للماريجوانا والامفيتامين على وظائف الكبد والكلى.

أجريت الدراسة على (40) فرد من مدمني الماريجوانا (THC) والأمفيتامين (AMP) و15 عينة كمجموعة سيطرة، واستغرقت الدراسة ثلاث أشهر للفترة 2021/5/23 - 2021/8/22. جمعت العينات من مدينة الصدر الطبية في النجف لتحديد تأثير تعاطي الماريجوانا (THC) والأمفيتامين (AMP) على وظائف الكبد والكلى. تتغير الكيمياء الحيوية (AST، ALT، ALP، اليوريا والكرياتينين) التي يمكن أن تحدث لمدمني مثل هذه الأدوية والدراسة الجينية للمدمنين.

وجد أن تعاطي الماريجوانا (THC) والأمفيتامين (AMP) اللذين لهما تأثير على إنزيمات الكبد(AST & ALT) ظهرت زيادة معنوية (P≤0.05) في مجموعة التعاطي عند مقارنتها بمجموعة السيطرة في نشاط الإنزيمات ، هناك زيادة ملحوظة في نشاط إنزيم AST (44.952±3.67) عند مقارنته بالمجموعة السيطرة (26.133±1.38) ، بينما كان نشاط إنزيم ALT أيضًا زيادة كبيرة (P≤0.04) ، ومستوى ALT أعلى في مصل مجموعة العينة (52.717±5.414) عند مقارنته بالمجموعة السيطرة (34.4±2.332) ، وأظهرت نتائج إنزيم ALP زيادة معنوية (P≤ 0.001*) في فعالية إنزيم الفوسفاتيز القلوي في المرضى (140.323±3.971) بالمقارنة مع المجموعة السيطرة (107.8±9.83).

أظهرت نتيجة وظائف الكلى أن هناك زيادة غير معنوية (P>0.05) في معدل اليوريا في الدم لمجموعة متعاطي المخدرات زيادة طفيفة (28.273±1.173) بالمقارنة مع المجموعة السيطرة (26.533±1.74) بينما أظهر مستوى الكرياتينين أيضا عدم - زيادة معنوية (P<0.408) في كرياتينين مصل الدم للمجموعة المعرضة للتعاطي (0.814) و (0.76) في مصل العينة الضابطة.

نستنتج من الدراسة الحالية ان تعاطي المخدرات تؤثر على وظائف الكبد والكلى ويؤدي مستقبلا الى امراض الكبد الحادة والفشل الكلوي.

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة بابل- كلية العلوم

قسم علوم الحياة

العلاقة بين ألادمان بالماريجوانا (THC) والأمفيتامين (AMP) مع وظائف الكبد والكلى

بحث مقدم الى كلية العلوم /جامعة بابل

وهو جزء من متطلبات نيل درجة الدبلوم العالي في العلوم /الادلة الجنائية

من قبل

منار جميل كاظم محمد

(بكالوريوس علوم حياة /جامعة الكوفة/ 2005)

اشراف

ا.م. د ازهار حمزة حسن

1443هـ 2021م