Prevalence And Early Prediction Of Acute Kidney Injury Among Drug Abuse Intoxicated Cases Admitted To Poison Control Center Ain Shams University Hospitals

Thesis

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قَالُوا سُبْحَانَكَ

لاَ عِلْمَ لَنَا

إِلاَّ مَا عَلَّمْتَنَا

إِنَّكَ أَنتَ

الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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Hisham mohammed abd elsami℮

Contents

List of Abbreviations

ACE-I	:	angiotensin-converting enzyme inhibitors
ACMD	:	Advisory Council on the Misuse of Drugs
AIN	:	acute interstial nephritis
AKI	:	Acute kidney injury
AKIN	:	Acute Kidney Injury Network
ARBs	:	angiotensin II receptor blockers
ATN	:	acute tubular necrosis
BPH	:	benign prostatic hypertrophy
BZS	:	Benzodiazepines
CAPMAS	:	Central Agency for Public Mobilization And Statistics
CB receptor	:	Cannabinoid receptor
CBHSQ	:	Center for Behavioral Health Statistics and Quality
CDC	:	Centers for Disease Control and Prevention
CHF	:	congestive heart failure
CIN	:	contrast-induced nephropathy
CK	:	creatine kinase
CKD	:	chronic kidney disease
CPB	:	cardiopulmonary bypass
DM	:	diabetes mellitus
DSM	:	Diagnostic and Statistical Manual of Mental Disorders
EMIT	:	enzyme multiplied immunoassay technique
ESRD	:	end stage renal disease on regular dialysis
FENa	:	fractional excretion of sodium
GC-MS	:	gas chromatography-mass spectroscopy
GCS	:	Glasgow coma scale
GFR	:	glomerular filtration rate
GSMH	:	General Secretariat of Mental Health

ICUs	:	intensive care units
IV	:	Intravenous
KDa	:	Kilodalton
KDIGO	:	Kidney Disease Improving Global Outcomes
MDMA	:	Methylenedioxymethamphetamine
MDRD	:	Modification of Diet in Renal Disease
MMWR	:	Morbidity and mortality weekly report
NCSCR	:	National center for social & criminology research
NGAL	:	Neutrophil gelatinase-associated lipocalin
NICE	:	National Institute for Health and Excellence
NIDA	:	National Institute on Drug Abuse
NSAIDS	:	nonsteroidal anti-inflammatory drugs
NSDUH	:	National Survey on Drug Use and Health
pNGAL	:	plasma Neutrophil gelatinase-associated lipocalin
RIFLE	:	Risk, Injury, Failure, Loss and End-stage renal disease
RRT	:	renal replacement therapy
SAMHSA	:	Substance Abuse and Mental Health Services Administration
SD	:	Standard deviation
SSRIS	:	Selective serotonin re-uptake inhibitors.
SUD	:	Substance Use Disorder
THC	:	tetrahydrocannabinol
U.S	:	united States
UNGAL	:	urinary Neutrophil gelatinase-associated lipocalin
UNODC	:	United Nations Office of Drugs and Crime
WHO	:	World Health Organization

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Abstract

Background: Drug abuse is a major social problem of the modern world as it is very common. It is estimated that a total of 246 million people, or 1 out of 20 people between the ages of 15 and 64 years, used an illicit drug in 2013. The majority of these illicit drugs or their metabolites are excreted through the kidneys and renal complications of drug abuse are very common. Early diagnosis and prompt treatment can significantly decrease morbidity and mortality in patients with acute kidney injury (AKI). AKI is currently diagnosed by functional biomarkers, such as serum creatinine measurement and estimation of urine flow rate. However, an elevation in serum creatinine is noticed only when GFR has already reduced below 50% of normal. Consequently, more reliable biomarkers than creatinine are necessary for both an accurate evaluation of renal function and an early detection of AKI.

Aim of the study: To study the prevalence of acute kidney injury among drug abuse intoxicated cases and to evaluate the role of neutrophil gelatinase associated lipocalin (NGAL) as an early predictor biomarker of acute kidney injury in such patients.

Patient and methods: This study is a prospective observational study performed at Poison control Center Ain Shams University was conducted on 75 drug abuse intoxicated patients during a period of 6 months from November 2016 to April 2017. Patients who developed AKI according to KDIGO criteria were assigned to the AKI group ($n = 20$), and those without AKI were assigned to the non-AKI group (n =55).

Results: On comparison of renal function of drug abuse intoxicated patients who developed AKI with non AKI group the serum creatinine and serum urea of these patients started to rise significantly within the 3rd day of admission while AKI patients in our study were significantly higher in serum and urinary NGAL in the first day of admission than Non- AKI which reflects the potential role of plasma and urinary NGAL as an early biomarker in predicting AKI.

Conclusion: Both serum NGAL and urinary NGAL levels measured at admission in drug abuse intoxicated patients can predict an occurrence of AKI for up to 72 hours of hospital stay with the cut-off points of 262.5 ng/ml and 84.5 ng/ml respectively.

GFR: glomerular filtration rate, **AKI:** Acute kidney injury, **NGAL:** Neutrophil gelatinase-associated lipocalin

INTRODUCTION

Drugs are the natural or synthetic substances that are used for medical purposes however, the repeated use of some of these leads to transient or chronic dependency *(Murthy et al., 2010).*

Drug abuse has become a major social problem of the modern world as it is very common it is estimated that a total of 246 million people, or 1 out of 20 people between the ages of 15 and 64 years, used an illicit drug in 2013 *(UNODC., 2013).*

The WHO reported that the prevalence of drug abuse in individuals between 15 and 64 years of age in Egypt was 0.8% (0.64 and 1.3% of drug abusers were found to be in the female and male population, respectively)*(WHO.,2010).*

The National Addiction Survey's in Egypt 3rd phase which was carried out by the General Secretariat of Mental Health (GSMH) between the years 2005 – 2007, covered 8 governorates, representing 0.25% of the target population. The study showed 9.8% of total used an addictive substance at least once, 3.1% of that total had used experimentally, 4.8% regularly used and 1.6% were dependent on substances. The most common substances were cannabis and its derivatives with 93.5%, alcohol and its derivatives 22.6%, pharmaceutical drugs 11.7%, opiates and its derivatives 7.3%,

amphetamines 5.3%, and synthetic drugs 0.31% *(Hamdi et al., 2009).*

The majority of these illicit drugs or their metabolites are excreted through the kidneys and renal complications of drug abuse are very common. It includes a wide range of glomerular, interstitial and vascular diseases. The damage may be acute and reversible, or chronic and can leads to end stage renal failure. The involvement of the kidney due to drug abuse is either attributed to their elimination through the kidney, or a direct nephrotoxic effect *(Pantelias et al.,2011).*

Acute kidney injury (AKI) is characterized by abrupt or rapid decline of renal function and is usually associated with the development of serious complications as well as an independent risk of mortality in hospitalized patients *(Coca et al.,2007).*

AKI develops in up to 5% of the hospitalized patients and in up to 30% patients admitted in the Intensive Care Unit. It is estimated that about 2 million people die of AKI every year. Those who survive AKI have a higher risk for later development of chronic kidney disease *(Jha et al., 2008).*

Early diagnosis and prompt treatment can significantly decrease morbidity and mortality in patients with acute kidney injury (AKI). AKI is currently diagnosed by functional biomarkers, such

as serum creatinine measurement and estimation of urine flow rate. However, as creatinine is primarily a marker for estimation of glomerular filtration, it cannot be considered for the estimation of kidney injury, since it is insensitive and unreliable to diagnose renal tubular injury in the absence of significant reduction in glomerular filtration rate (GFR)*(McCullough, et al.,2010).*

An elevation in serum creatinine is noticed only when GFR has already reduced below 50% of normal. Consequently, more reliable biomarkers than creatinine are necessary for both an accurate evaluation of renal function and an early detection of AKI**.**

AIM OF THE WORK

The aim of the work is to study the prevalence of acute kidney injury among drug abuse intoxicated cases admitted to poison control center Ain Shams University Hospitals and evaluate the role of neutrophil gelatinase associated lipocalin **(NGAL)** as an early predictor biomarker of acute kidney injury in such patients.

Chapter **(1):**

Substance use disorder

What Is Substance Use Disorder?

The term *substance use disorder* refers to a condition in which an individual's recurrent use of alcohol and/or drugs causes significant behavioral, physical, social, and psychological deterioration**(American Psychiatric Association, 2013).**

According to the Diagnostic *and Statistical Manual of Mental Disorders* (DSM*)*, a diagnosis of substance use disorder is based on a "pathological pattern of behaviors" related to substance use **(American Psychiatric Association, 2013a)**, some of which may be cravings or unsuccessful trials to control or decrease the use of alcohol or other drugs.

According to the *DSM* criteria, the National Institute on Drug Abuse has also compiled a list of these pathological or problematic behaviors (e.g., spending a lot of effort and time to obtain, use, or recover from the substance; or using the substance continuously in physically dangerous situations)**(NIDA ,2014).**

Other government sources have compiled their own lists as well. For example, the MentalHealth.gov *website* **(U.S. Department of Health and Human Services, n.d.)** provides a list of symptoms including.

 Physical changes: red eyes, sudden weight gain or loss, slurred speech.

- Behavioral changes: altered mood, lack of motivation, suspicious or secretive activities.
- Social changes: loss of friends, unexplained need for money.

Illicit drugs are drugs whose non-medical use has been prohibited by international drug control treaties *(Babor Tf et al., 2010)*, they include the plant-based drugs heroin, cocaine, and cannabis, synthetic drugs such as amphetamines, and pharmaceutical drugs such as opioids and benzodiazepines.

Prescription drug abuse nowadays is a worldwide problem of increasing concern to governments and the United Nations *(UNODC, 2011)*.

Global Health Problem

It is estimated that in 2012, between 162 million and 324 million people, corresponding to 3.5 per cent and 7.0 per cent of the world population aged 15-64, had used an illicit drug - mainly a substance belonging to the cannabis, opioid, and cocaine or amphetamine-type stimulants group - at least once in the previous year. The extent of problem drug use - by regular drug users and those with drug use disorders or dependence ranges between 16 million and 39 million people *(UNODC, 2014)*.

Worldwide substance use, which includes alcohol, nonmedical use of prescription medications, as well as illicit substance use, is increasing. According to a report by the United Nations Office of Drugs and Crime *(UNODC, 2014)* 162 to 324 million people use these substances; approximately 10% of them