# Evaluation of toxicological effects of ketamine and ethanol on the kidney of albino rats. Biochemical and Histopathological study

**Omima R. Mohamed,[1] Marwa M. M. Fawzy[1].**

**KEYWORDS**
*Ketamine,*
*Special K,*
*Kit-Kat,*
*Ethanol,*
*Abuse,*
*MDA,*
*Renal.*

## ABSTRACT

**Recently, abusers have begun using ketamine for recreation and dissociation, which is known among them by other famous street names such as Kit-Kat, Special K, Thirty-two-hole, Super K, Cat Valium, and Special Klub when combined with ethanol. The aim of this study is to evaluate the toxicological effects of ketamine and ethanol administration on the kidneys of albino rats (a biochemical and histopathological study). The total study period was 4 weeks. Thirty-two adult albino rats were divided into four groups, as follows: control group (Group I): eight rats received intraperitoneal (IP) 1.0 ml of 0.9% saline solution and by gavage 1.0 ml of distilled water; group II: eight rats received (IP) ketamine (25 mg/kg/d) diluted in 0.9% saline solution and by gavage 1.0 ml of distilled water; group III: eight rats received (IP) 1.0 ml of 0.9% saline solution and by gavage (5g ethanol/kg body weight/24h); and group IV: eight rats received (IP) ketamine (25 mg/kg/d) diluted in 0.9% saline solution and by gavage (5g ethanol/kg body weight/24h). This study assessed blood urea and creatinine levels, oxidative stress indices, determination of the level of malondialdehyde (MDA) in renal tissue, and histopathological examination of kidney tissue with a light microscope and transmission electron microscope (T.E.M.). Results showed an increase in blood urea and serum creatinine levels with degenerative changes in the kidney.**

## Introduction

Ketamine is one of the drugs used in the anesthesia of humans and is used mainly in veterinary processes. It is also used for child anesthesia and as a conscious tranquilizer in patients with asthma. Recently, abusers have begun using ketamine in recreation and dissociation, which is known among them by other famous street names such as Kit-Kat, Special K, K Hole, Super K, Cat Valium, Cat Tranquillizer, vitamin K, and known as Special K Lub when it is combined with ethanol (Jang et al., 2017; Paulis et al., 2020).

Ketamine is mainly used as a drug for anesthesia in poor countries because it requires less postoperative examination equipment. In addition, it is also commonly used in the veterinary process for huge and small domestic animals and wild animals (Gales and Maxwell, 2018).

Ketamine can cause sedation with a feeling of calmness and relaxation; it also leads to immobility, relief from pain, and amnesia with forgetfulness of events that occurred while the person was under the influence of the drug, so it is used as a rape drug. and it is abused for its dissociative sensations. Ketamine has been used in the USA as a recreational drug since the early 1990s. It is a restricted substance categorized in Schedule III of the restricted Substances Act. (Jhang et al., 2015).

[1] *Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Benha University, Egypt.*
*** Corresponding Author:** Omima R. Mohamed.
**Email:** omimarefaat1331@gmail.com

Recently, the number of abusers of ketamine who suffer from dangerous lower urinary tract symptoms and ulcerative cystitis has increased. It was found that it causes hydronephrosis of multiple degrees and kidney function affection. Clinical monitoring illustrates that long-term use of ketamine may lead to ureteral stenosis and hydronephrosis, which can be reversed by internal Double-J stenting (Lee et al., 2015).

It is well known that the toxicity of a substance can change when other substances are used with it. As we can be exposed to two or more xenobiotics in our lives and/or under work conditions, the study of interactions between toxic materials is an important issue in recent toxicology (Gupta and Gill, 2000).

The abuse of psychoactive substances is considered a traditional and universal act and is related either to the culture or to religious rituals. An increasing abuse of recent psychoactive materials has been found, and the common finding of the simultaneous taking of multiple substances leads to the term "polydrug." A common example is the abuse of ethanol with other stimulants and/or drugs of hallucination, such as ketamine (Mendes et al., 2017).

Ethanol is widely used as a beverage in multiple countries, so multiple studies have gradually illustrated its harmful effects. It is eliminated from the body through a variet y of methods.
A portion of the ethanol is eliminated from th e body by breathing and a portion through uri ne. The mechanism of toxicity of ethanol in kidneys is directly related to the accumulation of free radicals due to oxidative stress, which causes structural damage and functional deterioration in kidneys (Jalili et al., 2019).

The aim of the current study is to study the toxicological effects of ketamine and ethanol administration on the kidneys of rats (a biochemical and histopathological study).

## Materials and methods

### *Animals:*

The number of rats in this study was thirty-two adult albino rats weighing 200 g. In the Faculty of Veterinary Medicine, all rats were adopted for one week by administering food and water without any drugs. All ethical considerations for animal treatment were followed according to the Ethics Committee of Scientific Research, Faculty of Medicine, Benha University (code: RC-22-5-2023).

### *Chemicals:*

Ketamine was purchased from Sigma Aldrich (St. Louis, MO, USA) as a pure hydrochloride without preservatives. Ethanol 10% was purchased from Sigma Aldrich (St. Louis, MO, USA).

### *Animals grouping:*

At the start, rats were separated into four groups as follows:

**Group I (control group):** 8 rats received saline solution 0.9% 1.0 ml for each rat intraperitoneally (IP) and received by gavage distilled water 1.0 ml for each rat.

**Group II:** 8 rats were given (IP) ketamine diluted in saline solution 0.9% (25 mg ketamine/kg/d) (Gass et al., 2014) and (Jang et al., 2017), as well as 1.0 ml gavage distilled water.

**Group III:** 8 rats received a saline solution of 0.9% 1.0 ml (IP) for each rat and

took oral (5 g ethanol/kg body weight/24 h) (Jalili et al., 2019*)*.

**Group IV:** 8 rats received IP (25 mg ketamine/kg/d) and took it orally (5 g ethanol/kg body weight/24 h).

Rats were treated for 4 weeks. By the end of the experiment, all remaining rats were sacrificed with anesthesia "after one day from the last dose", the abdomen and thorax were opened, and blood samples were collected from the abdominal aorta and processed for biochemical measurements. kidneys were taken for determination of the level of malondialdehyde (MDA) and for examination by electron and light microscope.

***Methods:***

**A) Biochemical study:** According to Pincus and Lifshitz (2007), renal functions (creatinine and urea) were determined using the commercial Spinreact Creatinie-J kit with spinlab (Spinreact Company), Spain.

**B) Oxidative stress indices:** Noiri et al. (2018) described the thiobarbituric acid method for determining the quantity of malondialdehyde (MDA) in renal tissue. After centrifugation, thiobarbituric acid (0.67%) was added to the supernatant of a sample of kidney tissue combined with 2.5 liters of 10% trichloroacetic acid. For 30 minutes, the mixture was immersed in boiling water. At 532 nm, the absorbance was determined (Chattopadhyay et al., 2003).

**C) Histopathological study:** sections were taken from the kidney and examined using hematoxylin and eosin (H&E) and a light microscope (OLYMPUS, Japan) at the pathology department in the Benha Faculty of Medicine. According to Lamberg and Rothstein (1978), the kidneys were promptly fixed in a 10% formalin solution for 5 days and stained with hematoxylin (Hx) and eosin medicine (E).

Examination by the electron microscope unit at Tanta University After the removal of the kidneys, they were fixed immediately in a glytrahyde solution. Then, several sections were taken, one micron thick (semithin section) using an ultra-microtome with glass knives. The sections were stained with toluidine blue and examined by a transmission electron microscope at 80 kilovolts.

**Statistical analysis:**

The data were analyzed using the SPSS program (Spss Inc., Chicago, Illinois), version 26. Descriptive statistics were calculated in the form of mean and standard deviation (SD) for quantitative data. and the significance of the difference was tested using one of the following tests: Student's t-test: a test used to compare the mean of two groups of quantitative data. and ANOVA test (F value): a test used to compare the means of more than two groups of quantitative data. A P value <0.05 was considered statistically significant (*), while a >0.05 statistically insignificant P value <0.01 was considered highly significant (**) in all analyses.

**Results:**

**A) Biochemical study:**

Our study revealed a highly significant ($p< 0.001$) difference in blood urea and creatinine levels between all studied groups (Table 1; Figures 1 and 2). Also, the study revealed a significant difference between the control and (ketamine, ketamine+ ethanol) groups, but there was no significant difference between the control group and the ethanol

group regarding urea level (Table 2). As regards comparison between test groups, the study revealed a non-significant difference between the ketamine group and the (ethanol, ketamine+ ethanol) groups, but there was a highly significant difference between the ethanol group and the ketamine+ ethanol group regarding urea level (Table 2).

**B) Malondialdehyde (MDA) kidney tissue level:**

Our study showed a highly significant ($p< 0.001$) increase in malondialdehyde (MDA) kidney tissue level `between all studied groups (Table 1; Figure 3). Also, the study showed a non-significant difference between the control group and the ketamine group; there was a significant difference between the control group and the ethanol group; and the study revealed a highly significant difference between the control group and the ketamine ethanol group (Table 2). As regards the comparison between test groups, there was no significant difference between the ketamine group and the (ethanol, ketamine+ ethanol) groups, but the study showed a significant difference between the ketamine group and the (ketamine+ ethanol) group (Table 2).

**Table (1):** Statistical comparison of urea, creatinine (mg/dl), and kidney MDA (nmol/g) between studied groups

| Parameter | Control group (n=8) | Ketamine group (n=8) | Ethanol group (n=8) | Ketamine + Ethanol group (n=8) | Test of significance | P value |
|---|---|---|---|---|---|---|
| **Urea** | | | | | | |
| **Mean ± SD** | 37.83±3.91 | 45.17±4.22 | 42.37±3.01 | 48.5±1.52 | | |
| **Median** | 37.0 | 44.0 | 42.50 | 48.5 | F=10.912 | <0.001* |
| **(Min-max)** | (34.0-45.0) | (40.0-52.0) | (38.0-46.0) | (46.0-50.0) | | |
| **Creatinine** | | | | | | |
| **Mean ± SD** | 0.65±0.19 | 1.13±0.18 | 0.93±0.12 | 1.14±0.23 | | |
| **Median** | 0.65 | 1.15 | 0.94 | 1.20 | F=9.370 | <0.001* |
| **(Min-max)** | (0.40-0.90) | (0.87-1.40) | (0.80-1.10) | (0.76-1.40) | | |
| **Kidney MDA** | | | | | | |
| **Mean ± SD** | 41.17±4.12 | 45.67±2.94 | 47.50±2.17 | 50.5±3.08 | | |
| **Median** | 40.0 | 45.0 | 48.00 | 51.0 | F=9.198 | <0.001* |
| **(Min-max)** | (38.0-49.0) | (42.0-50.0) | (44.0-50.0) | 46.0-54.0) | | |

n: number, SD: standard deviation, min: minimum, max: maximum, MDA: malondialdehyde, F: ANOVA test, P<0.001* highly significant, (mg/dl): milligrams/deciliter, nmol/g: mol/gram.

**Table (2):** Pair-wise comparison of urea, creatinine, and kidney MDA between studied groups

| Parameters | Control versus ketamine group | Control versus ethanol group | Control versus ketamine ethanol group | Ketamine group versus Ethanol group | Ketamine group versus Ketamine Ethanol group | Ethanol group versus Ketamine Ethanol group |
|---|---|---|---|---|---|---|
| **Urea** | T= 3.102 | T=2.212 | T=6.147 | T=1.340 | T=1.823 | T=4.480 |
| | P=0.011* | P=0.053 | P=0.001* | P=0.213 | P=0.116 | P=0.003* |
| **Creatinine** | T=4.473 | T=3.092 | T=4.077 | T=2.222 | T=0.125 | T=2.018 |
| | P=0.001* | P=0.014* | P=0.002* | P=0.055 | P=0.903 | P=0.081 |
| **Kidney MDA** | T=2.177 | T=3.333 | T=4.444 | T=1.228 | T=2.778 | T=1.950 |
| | P=0.057 | P=0.011* | P=0.002* | P=0.250 | P=0.020* | P=0.083 |

T: Independent t-test, *statistically significant P value <0.05 was considered statistically significant while >0.05 statistically insignificant, P<0.001* highly significant, K: Ketamine, E: Ethanol, MDA: malondialdehyde.

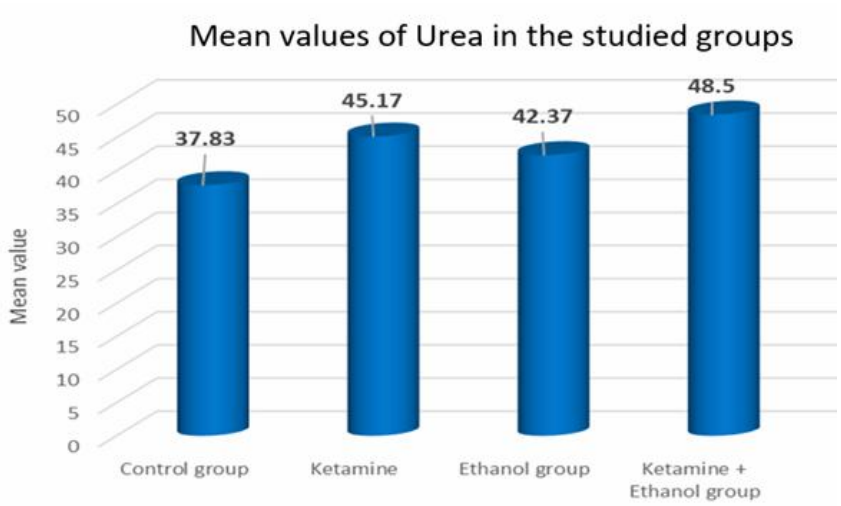


**Fig. (1):** Comparison between the studied groups according to urea level.

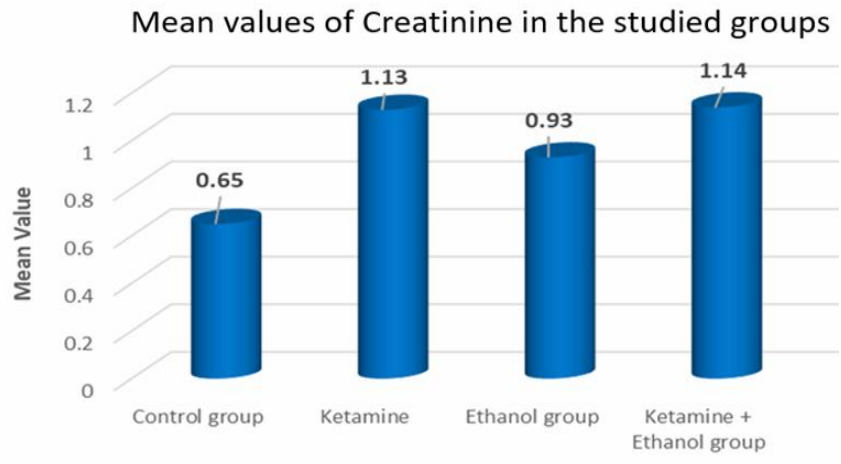


**Fig. (2):** Comparison between the studied groups according to serum creatinine level.

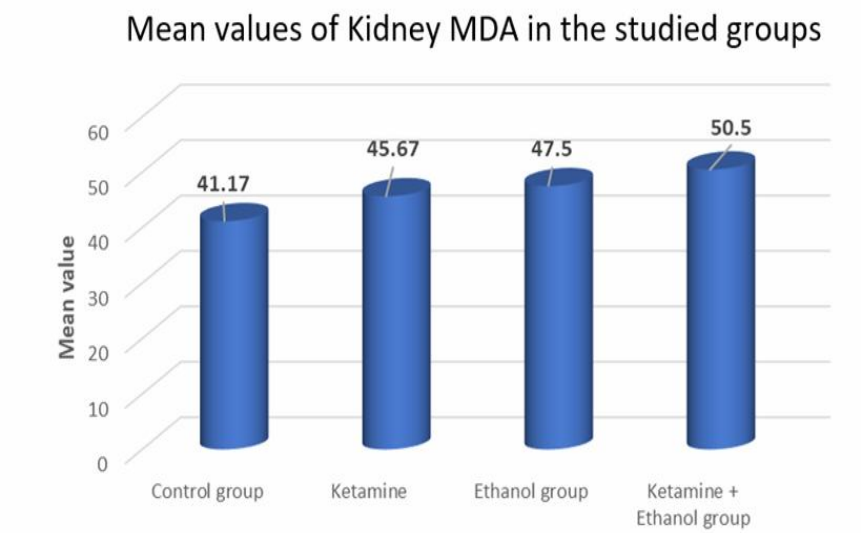


**Fig. (3):** Comparison between the studied groups according to MDA level.

**C) Histopathological results:**

Sections of the kidneys of the control group were examined under a light microscope showing a normal structure of kidney corpuscles and tubules. The kidney corpuscle has a blood capillary tuft that is bordered by two layers of Bowman's membrane that surround the glomerulus capsule and the urinary gap in between. The kidney proximal convoluted tubules and distal convoluted tubules were normal (Figure 4a).

Sections of rats' kidneys in the ketamine group showed moderate renal tubular epithelium damage with a wide lumen and infiltration of inflammatory cells with extravasation of RBCS (Figure 4b). Sections of rats' kidneys in the ethanol group showed moderate renal corpuscle and tubule damage, where atrophied some kidney corpuscles with glomerular tuft shrinkage and dilatation of the kidney space and damage to the epithelium of tubules, wide lumen, and blood vessels were congested (Figure 4c). Sections of rats' kidneys in the ketamine ethanol group detected severe damage in the renal corpuscles and tubules, including atrophied renal corpuscles with shrinkage of glomerular tufts and dilatation of the kidney space, along with damage to the epithelium of tubules, luminal widening, and infiltration of mononuclear cells, as shown in figure 4d.

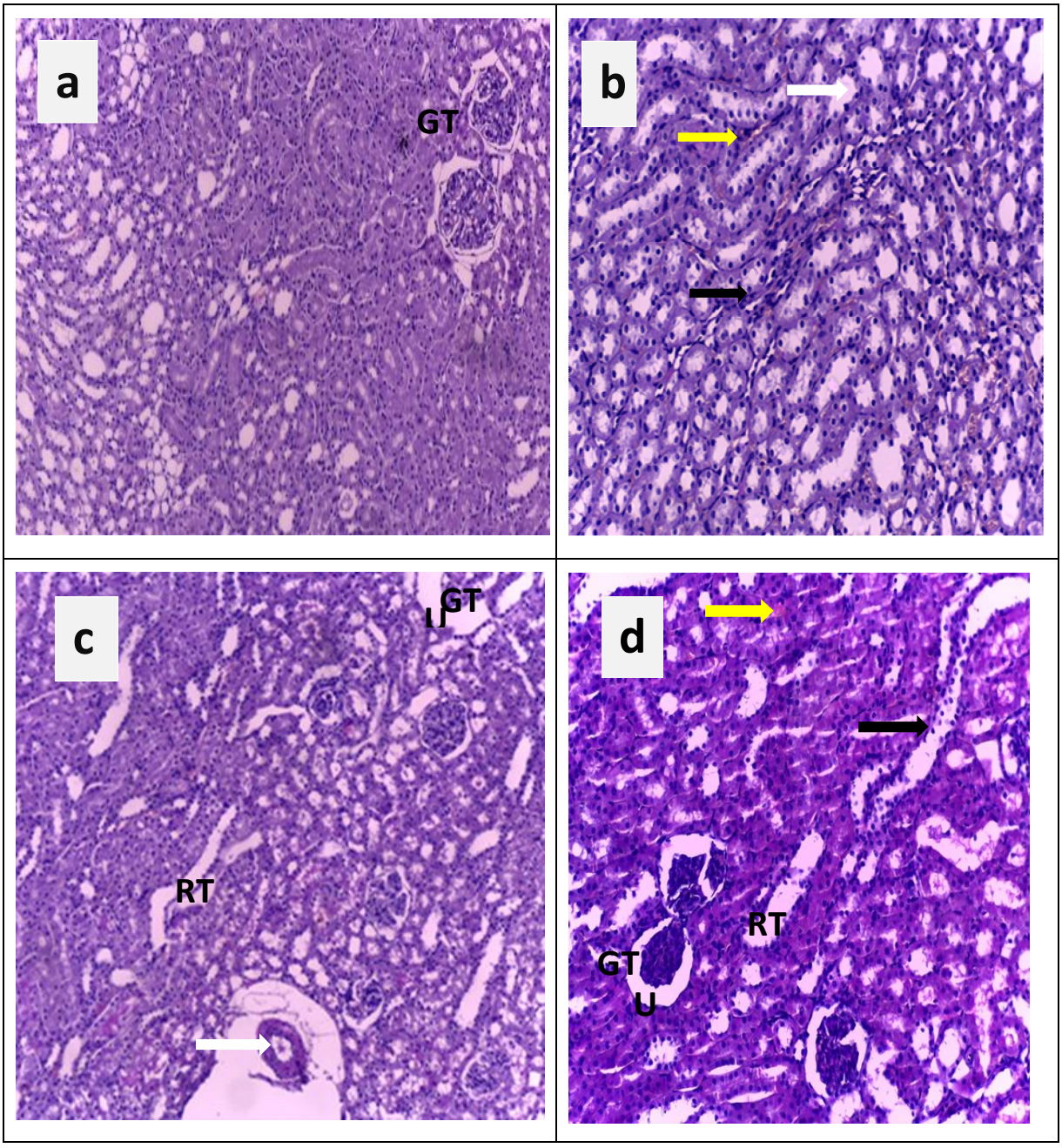


**Fig. (4):** Histopathological evaluation of rat's kidneys: (a) The control group showed normal kidney architecture. M: X100 (b) in the ketamine group, tubular epithelial degradation with lumen expansion (white arrows) and inflammatory cell infiltration (black arrows) with RBCS extravasation (yellow arrows). M: X200, (c) renal corpuscles atrophied with shrinkage in glomerular tuft (GT) and dilatation in kidney space (U), damage to the epithelium of kidney tubules with a wide lumen (RT), and congestion of blood vessels (white arrow) in the ethanol group M: X100, (d) renal corpuscles atrophied with shrinkage in glomerular tuft (GT) and dilatation in kidney space (U), Hydropic damage to epithelium of kidney tubules with widening of lumen (RT) and hydropic damage of epithelium (black arrow) extravasation of RBCS (yellow arrows) in the ethanol + ketamine group. M: X200

### D) Electron microscopic results:

Sections taken from the kidney of the control group and examined by electron microscopy revealed a normal proximal convoluted tubule with a regular nucleus and a complete brush border (Figure 5a). The ketamine group showed irregular nuclei, irregular brush border changes, and vacuoles in mitochondria and cytoplasm (Figure 5b). The ethanol group showed a nucleus irregular and deformed with rarefaction, vacuoles in mitochondria and cytoplasm, and a deformed brush border (Figure 5c). The ketamine and ethanol groups revealed a nucleus that is irregular and deformed with rarefaction; vacuoles in mitochondria and cytoplasm; and a brush border was lost (Figure 5d).

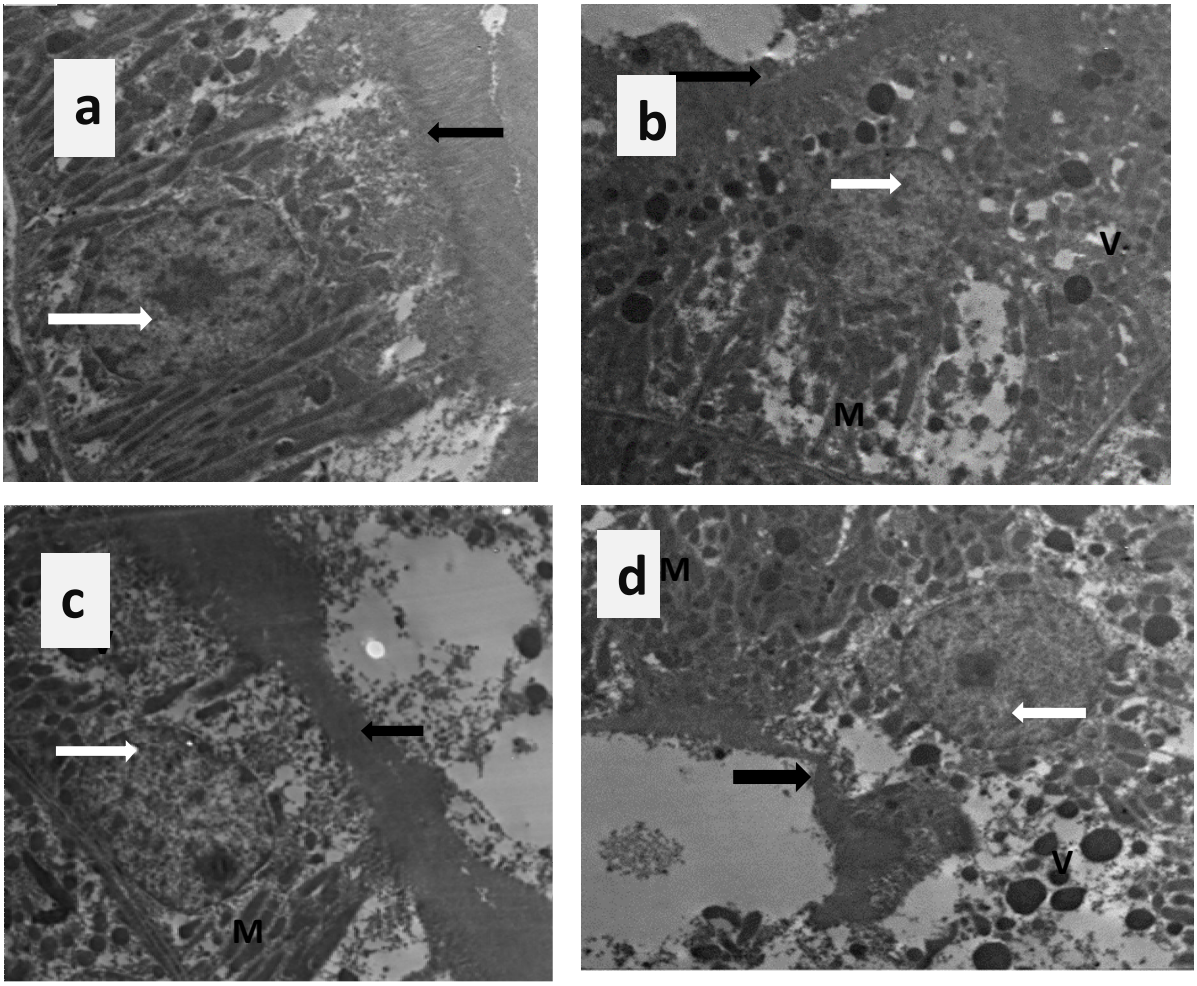


**Fig. (5):** Proximal convoluted tubules of rat kidneys examined by electron microscopy: (a) control group was normal, M 2000 (b) deformed nucleus (white arrow), irregular brush border (black arrow), mitochondria (M) showing deformation, and vacuoles cytoplasm showing vacuoles (V) in the ketamine group. M:2000, (c) deformation of nucleus (white arrow), changes and vacuoles in mitochondria (M), cytoplasm showing vacuoles (V) and irregular brush border (black arrow) in the ethanol group Ib.M:2000, (d) deformation in nucleus (white arrow), changes and vacuoles in mitochondria (M), cytoplasm showing vacuoles (V) and absent brush border (black arrow) in ketamine + ethanol group. Magnification: X2000.

**Discussion:**

The current study aimed to evaluate the toxicological effects of ketamine and ethanol administration on the kidneys of rats (a biochemical and histopathological study). The term polydrug abuse is increasing. For example, ethanol's use as an illicit beverage is commonly, taken simultaneously with multiple types of illegal materials named "club drugs", which are always in change. Ketamine is one of these materials (Mendes et al., 2017).

The kidney is the most affected organ by the toxic hazard as it has high blood flow due to its role in the concentration of urine and its role in the activation of xenobiotics, so it is exposed to the blood-borne toxicant to a greater extent than other organs (Gwaltney, 2018).

The results of the present study revealed the absence of any abnormal findings among rats in the control groups as regards biochemical studies. Also, there were no abnormal histopathological changes in the renal tissues of the adult albino rats in these groups throughout the study period. However, results showed a significant increase in levels of urea and creatinine in all test groups in comparison to control groups. Mendes et al. (2017) showed in their study that long-term ethanol usage significantly increased levels of urea and creatinine in rats receiving ethanol (1.6 g/kg) daily for 12 weeks, and their findings are consistent with ours.

Also, multiple studies on ethanol with different dosages and periods showed impairment of kidney function as it presents in beverages by different percentages, which may reach 50%. Rezende and Mama (2015) found an increase in creatinine levels in dogs given ketamine in combination with 12% ethanol in drinking water for one month, but with no rise in blood urea levels, indicating absence of renal impairment. Shirpoor et al. (2016) discovered that prolonged ethanol exposure impairs kidney function, as evidenced by a significant increase in plasma creatinine, urea, cystatin C levels, and the cystatin C/creatinine ratio. Furthermore, there was a significant decrease in creatinine clearance as an indicator of glomerular filtration rate in the ethanol-treated group by 4.5 g for 6 weeks compared to the control group. Another study was conducted on 6529 adults for 5 years, revealed that persons who were mild alcohol drinkers (10-30 grams daily) or severe drinkers (more than 30 grams daily) had an increased risk for albuminuria; an indication of rapid loss of kidney function (White et al., 2009).

Sub-chronic toxicity of the ethanol leaf extract of Syzygium guineense in rats showed that the serum urea level in male rats did not vary significantly between the treatment and control groups. However, elevated serum urea levels were recorded in female rats treated with 500 mg/kg (80.3 ± 7.8) and 1000 mg/kg (72.2 ± 13.0) of the plant extract. (Loha et al., 2019).

In the present study, there was an increase in malondialdehyde (MDA) kidney tissue levels in all test groups. These findings are comparable to those of Jalili et al. (2019), who discovered a substantial increase in serum MDA levels in rats after consuming (5 g EtOH/kg body weight/24 h) by gavage daily for 12 weeks. Also, Patki et al. (2013) found an increase in NO and MDA in the hippocampus, which demonstrates that the administration of intermittent ketamine generates cell damage.

In addition, oral treatment of rats to a large amount of ethanol (5 g/kg) for three hours resulted in an increase in malondialdehyde activity, superoxide dismutase, renal corpuscles, and dilatation and congestion of the peritubular arteries

(Sonmez et al., 2012). The study by Paulis et al. (2020) showed that ketamine caused lipid peroxidation, which mirrored increased MDA levels in rats treated with ketamine for 6 weeks.

Ketamine could cause kidney injury by inhibiting adenosine receptors, which could impair the regulation of glomerular filtration and kidney blood flow (Rajandram et al., 2017). Jhang et al. (2015) proposed that hydroquinone, a possible ketamine metabolite that can directly fragment DNA and chromosomes in cells, plays a critical role in ketamine pathogenesis, so more research into hydroquinone urine concentrations is needed to prove this as a cause of ketamine pathogenesis.

Ethanol may cause kidney injury by increasing the synthesis of lipid peroxidation in kidney cells, which leads to DNA breakage and histopathological damage (Jalili et al., 2019). The frequent ethanol exposure led to the production of oxidative stress, which induced histological damage. Ethanol leads to kidney damage through its biological effect by electrophilic cells in the kidneys attacking and producing ROS (Tsai et al., 2017). In a study of acute alcohol intoxication by injections of 5 g/kg ethanol to rats over 3 h, the major finding of this study was that heavy alcohol intoxication before glycerol-induced rhabdomyolysis exacerbates organ damage (Tsai et al., 2017).

In our study, the histopathological changes matched with biochemical changes, as slides of the kidneys of rats in all test groups, in comparison to control groups, showed kidney corpuscle necrosis with shrinkage of the glomerular tuft, and large kidney space, damage of the kidney tubules, and inflammatory cell infiltration with extravasation of RBCs.

Rajandram et al. (2017) discovered mononuclear inflammatory cells in between tubules in a rat receiving 100 mg/kg illicit ketamine combination and renal papillae with evidence of fibrosis between the tubules in a rat receiving 300 mg/kg illicit ketamine in their study of oral illicit ketamine administration to rats for 4 weeks.

Jang et al. (2017) showed in a study on rats receiving ketamine (25 mg/kg/d, intraperitoneally) through daily injections for a period of 14 days and 28 days' increase in the formation of collagen type I and fibronectin in the kidneys of ketamine-treated rats, and the increase in the production of collagen type I led to bladder hypertrophy as Type I collagen is the largest collagen in the body. Masson's trichrome stain also showed collagen accumulation in the interstitial tissues of the renal cortex, denoting an increase in renal interstitial fibrosis. Chung et al. (2010) observed macrophages increasing in ischemic tissues to eat debris and dead cells and to remodel the tissue matrix.

Adisa et al. (2019) showed in their study of the sub-acute effect of ethanol on the kidney tissue of albino rats after 28 days' administration of ethanol extracts of ASE stem bark. widening of Bowman's space, damage of cortex tubules, and severe change in all kidney tissue, and these histopathological results matched our results.

Jalili et al. (2019) showed that in their study, the rats after taking (5 g EtOH/kg body weight/24 h) gavage daily for 12 weeks increased Bowman's capsule space, the distribution of lymphocytes bleeding in the space between the tubules, and the formation of adipose tissue.

Alcohol reduced kidney function and caused renal tissue damage in rats, including swelling of cells and mitochondria in the proximal renal tubules, cellular damage in the distal renal tubules and loops of Henle, luminal widening, and edema and fibrosis in the interstitium. These results matched our

results, which revealed that large ethanol consumption has kidney toxicity (Tasi et al., 2017).

## Conclusion:

This study revealed that ketamine and ethanol administration result in kidney injury. This is demonstrated by alterations in renal function and an increase in MDA, both of which correspond to histopathological damage. So, in cases of kidney affection without knowing the cause, we must take a history of ketamine and ethanol use.

## Recommendations:

Ketamine users and those with chronic alcoholism should be subjected to multiple laboratory follow-ups of kidney functions.

Continuous use of ketamine and ethanol must be avoided.

Other experimental studies are needed in order to understand the toxicity of each drug.

Awareness campaigns of hazards of ketamine and alcohol abuse should be increased especially their toxic effects on kidney.

## Limitations:

The study period was 4 weeks to demonstrate subacute toxicity, which did not allow for studying chronic and withdrawal effects. We study toxicological effects on kidney organ only, so other studies on different body organs are needed.

**Conflicts of interest:** The authors have declared that no conflict of interest exists.

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## References:

**Adisa R.A., Kolawole N., Sulaimon L.A., et al. (2019)** "Alterations of antioxidant status and mitochondrial succinate dehydrogenase activity in the liver of Wistar strain albino rats treated with by ethanol extracts of Annona senegalensis Pers. (Annonaceae) stem bark". *Toxicology Research Journal*, 35, pp.13-24.

**Chattopadhyay A., Biswas S., Bandyopadhyay D., et al. (2003)** "Effect of isoproterenol on lipid peroxidation and antioxidant enzymes of myocardial tissue of mice and protection by quinidine'. *Molecular and Cellular Biochemistry*, 245, pp.43-49.

**Chung C.W., Zhang, Q.L. and Qiao, L.Y. (2010)** "Endogenous nerve growth factor regulates collagen expression and bladder hypertrophy through Akt and MAPK pathways during cystitis." *Journal of Biological Chemistary*, 285, pp.4206e12.

**Gales A. and Maxwell S. (2018)** "Ketamine: recent evidence and current uses". *ATOTW* , 2(381): pp. 1–7.

**Gass A. J., Schwarz, A., Sartorius., et al. (2014)** "Sub-anesthetic ketamine modulates intrinsic BOLD connectivity within the hippocampal-prefrontal circuit in the rat". *Neuro-psycho-pharmacology Journal*, 39 (4): pp.895–906.

**Gupta V. and Gill K. D. (2000)** "Influence of ethanol on lead distribution and biochemical changes in rats exposed to lead". *Alcohol Journal*, 20, pp. 9–17.

**Gwaltney S.M. (2018)** "Brant, renal toxicity". *Veterinary Toxicology Journal*, pp 259–272.

**Jalili C., Roshankhah R. and Salahshoor M. (2019)** "Falcaria vulgaris extract attenuates ethanol-induced renal damage by reducing oxidative stress and lipid peroxidation in rats cyrus". *Journal of Pharmacy and Bioallied Sciences* ,11 (3), pp. 268–275.

**Jang M.Y., Shen J. T., Geng J.H., et al. (2017) "**Ketamine induced renal fibrosis in a ketamine addition rat model". *Urological Medical Science Journal*, pp.123-127.

**Jhang J.F., Hsu Y.H., and Kuo H.C. (2015)** "Possible pathophysiology of ketamine-related cystitis and associated treatment strategies". *International Journal of Urology*, 22, pp.816—825.

**Lamberg L. and Rothstein R. (1978) "**Laboratory manual of histology and cytology". *Book*, p.140.

**Lee H.Y., Hsu Y.C., Hsu C.Y., et al. (2015)** "Upper urinary tract damage caused by ketamine snoringda report of nine cases". *Urological Science Journal*, 26, pp 182e5.

**Loha A., Mulu S.M, Abay W., et al. (2019)** "Acute and subacute toxicity of methanol extract of Syzygium guineense leaves on the histology of the liver and kidney and biochemical compositions of blood in rats". *Evidence-based Complementary and Alternative Medicine*:15 . DOI: 10.1155/2019/5702159.

**Mendes P. F., Simon K. A. and Hueza I.M. (2017)** "Toxic and immunotoxic valuation of ketamine and ethanol in rats during 28day". *International Journal of Pharmacy and Pharmaceutical Sciences*, 9(9) pp. 205-214.

**Noiri E., Nakao A., Uchida K., et al. (2018)** " Oxidative and nitrosative stress in acute renal ischemia". *American Journal of Physiology-Renal Physiology*, 281: pp.948–957.

**Pincus M.R. and Lifshitz M.S. (2007)** *Evaluation of Renal Function, Water, Electrolytes and Acid–Base Balance.* In: Henry's Clinical Diagnosis and Management by Laboratory Methods, Saunders Company, Philadelphia, U.S.A, (14) pp. 360-376.

**Patki G., Solanki N., Atrooz F., et al. (2013)** "Depression, anxiety-like behavior and memory impairment are associated with increased oxidative stress and inflammation in a rat model of social stress". *Brain Research*, 1539, pp. 73–86,

**Paulis M.G., Hafez E.M and El-Tahawy N.F. (2020)** "Toxicity and post withdrawal effects of ketamine on the reproductive function of male albino rats: Hormonal, histological, and immune-histochemical study". *Human and Experimental Toxicology Journal*, pp.1–12.

**Rajandram R., Ning Yi., YAP T., et al. (2017**) " Oral ketamine induced pathological changes of the urinary tract in a rat model" . *Malaysian Journal of Pathology*, 39(1) pp. 47 – 53.

**Rezende M., and Mama K., (2015)** "Anesthesia for patients with renal disease". *Clinial. Brief*, pp. 41-44.

**Shirpoor A., Rezaei F., Fard A.A., et al. (2016)**" Ginger extract protects rat's kidneys against oxidative damage

after chronic ethanol administration". *Biomed Pharmacother.* ,84 pp. 698–704.

**Sonmez M.F., Narin F., Akkus D., et al. (2012)** "Melatonin and vitamin C ameliorate alcohol-induced oxidative stress and eNOS expression in rat kidney". *Ren. Fail.*, 34, pp. 480-486.

**Tsai J., Chung-Jen L., Yi-Maun S., et al. (2017)** "Acute alcohol intoxication exacerbates rhabdomyolysis-induced acute renal failure in rats". *International Journal of Medical Science*, 14 pp. 680-689.

**White S.L., Polkinghorne K.R., Cass A., et al. (2009)** "Alcohol consumption and 5-year onset of chronic kidney disease The AusDiab study". *Nephrol. Dial. Transplant*, 24, pp. 2464-2472.

# تقييم الآثار السمية للكيتامين والايثانول في الجرذان البيضاء؛ دراسة كيميائية وهستوباثولوجية

**أميمة رفعت محمد السيد، مروة محمد مراد فوزى**

**قسم الطب الشرعي و السموم الاكلينيكية - كلية الطب - جامعة بنها**

أن تناول مواد مختلفة في وقت واحد يدعى بمصطلح "مخدرات متعددة" والمثال الشائع لذلك تعاطي الإيثانول مع المنشطات و أدوية الهلوسة الأخرى، مثل الكيتامين الذى قد زاد تناوله فى الأونة الأخيرة. وقد هدفت الدراسة الحالية إلى تقييم الاثار السمية لمادتى الكيتامين والايثانول على الكلى فى الجرذان البيضاء. الطرق: وكانت مدة الدراسة اربعة اسابيع. تم تقسيم ٣٢ من الجرذان البالغة إلى أربع مجموعات كما هو موضح: المجموعة الضابطة (٨ جرذان تم اعطائهم ١ مل/ل من محلول الملح عن طرق الحقن فى البريتون وا مل /ل من الماء المقطر عن طريق الفم) ؛ مجموعة الاختبار ١ (٨ جرذان تم اعطائهم ٢٥ مجم /كجم/يوميا من الكيتامين المذاب فى محول الملح عن طريق الحقن فى البريتون و ا مل /ل من الماء المقطر عن طريق الفم) ؛ مجموعة الاختبار ٢ (٨ جرذان تم اعطائهم ١ مل من محلول الملح عن طرق الحقن فى البريتون و ٥ جم /كجم/يوميا من الايثانول عن طريق الفم) مجموعة الاختبار ٣ (٨ جرذان تم اعطائهم ٢٥ مجم /كجم/يوميا من الكيتامين المذاب فى محول الملح عن طريق الحقن فى البريتونون و ٥ جم /كجم/يوميا من الايثانول عن طريق الفم) و قد قيمت الدراسة مستويات الكرياتينين واليوريا فى الدم ؛ هذا و قد تم أيضا فحص الكلى بواسطة المجهر الضوئي والمجهر الإلكتروني بالاضافة الى مؤشرات الإجهاد التأكسدي عن طريق تحديد مستوى المالونديالدهيد في أنسجة الكلى: و قد تبين من نتائج الدراسة الحالية ارتفاع في مستوى اليوريا والكرياتينين في الدم ، مع تغيرات تنكسية في التشريح المرضي للكلي في جميع مجموعات الاختبار.