Original Article

Assessment of Tissue Histotoxicity and Effective Dose of computed tomography (CT) Contrast Media

Ammar Alhasan[1], Safa Azhar Razzaq[1], Ahmed Adeeb Mohamed[1], Aiad Gaber Arean[2], Tammar Hussein Ali[1]

[1]College of Pharmacy, Al Muthanna University, Samawah, Al-Muthanna, Iraq, [2]Clinical Oncology Unit, Faculty of Medicine, Al Muthanna University, Samawah, Al-Muthanna, Iraq

Abstract

Background: A computed tomography (CT) scan is one of the most prevalent techniques used for disease diagnosis. Clinically, CT scans might necessitate contrast media (CM) to enhance the clarity of images of different tissues and organs. Presently, iodinated contrast is widely utilized despite several drawbacks. The main current concern is regarding the potential toxicity of combining a high effective dose with CM injection in CT imaging diagnosis. **Objectives:** This study represents two main areas: first, measurement of risks of CT radiation to the diagnostic organ. Second, it scrutinizes the histotoxicity of CM. **Materials and Methods:** This study involves *in vitro* and *in vivo* assessment of the measured doses' effectiveness and histotoxicity effects of CM in CT imaging. The main focus lies in evaluating the histotoxicity impact of intravenously injected CM on animals. Furthermore, the assessment of collecting blood samples was evaluated for human patients. **Results:** CM impact was validated through injected animals to evaluate its effect on kidney function. Outcomes indicate no deterioration but a slight increment in creatinine levels. CT examinations were examined for patient diagnosis, revealing a significant correlation between the patient's age and effective dose ($P < 0.05$); a higher effective dose was observed in 15–30-year-old patients; however, there are no significant gender-based distribution differences. **Conclusion:** These findings highlight the critical need to strike a careful balance between the advantages of diagnostic efficacy and the potential risks linked with CM-enhanced CT imaging. This is crucial in the optimization of protocols to mitigate radiation exposure, maintaining diagnostic accuracy and ensuring patient safety.

Keywords: Contrast media, CT imaging, effective dose, histotoxicity, iohexol

Introduction

The escalating concern surrounding radiation dose in correlation with contrast media (CM) in computed tomography (CT) scans primarily stems from histotoxity, in addition to the impact of effective dose (ED).[1-4] Commercial CM, extensively employed in CT imaging, have been playing a crucial role in enhancing image quality and offering high-resolution images.[5,6] However, it has been reported that these CM suffer from drawbacks such as short blood retention, high concentration, limited enhancement, and nonspecific detection and localization.[7-9] Moreover, drug interaction may occur between contrast agents and some other medications that are generally taken. A total of 585 drugs are known to interact with CM, resulting in 475 major drug interactions; meanwhile, 110 moderate drug interactions have been observed.[10] Side effects of contrast agents can be differentiated into general and renal reactions. It was revealed that the incidence and severity of these contrary responses are correlated with physical reasons such as the "osmolality" of CM existing.[11] Even though regularly used in clinical diagnosis, CM possess adversarial special effects, particularly severe on

Access this article online

Quick Response Code:

Website: https://journals.lww.com/mjby

DOI: 10.4103/MJBL.MJBL_808_24

Address for correspondence: Dr. Ammar Alhasan, College of Pharmacy, Al-Muthanna University, Samawah 66001, Al-Muthanna, Iraq.
E-mail: ammar.physicist@gmail.com
Dr. Tammar Hussien Ali, College of Pharmacy, Al-Muthanna University, Samawah 66001, Al-Muthanna, Iraq
E-mail: tammar@mu.edu.iq

Submission: 02-Oct-2024 **Accepted:** 01-Dec-2025 **Published:** 23-Jan-2026

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 License (CC BY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Alhasan A, Razzaq SA, Mohamed AA, Arean AG, Ali TH. Assessment of tissue histotoxicity and effective dose of computed tomography (CT) contrast media. Med J Babylon 2025;22:1514-21.

patients' health with impaired renal functions relatively. Therefore, they are considered a major cause of acute renal failure. So, the injection of contrast agents for chronic kidney diseases (CKD), moderate to severe stage (3–5), was approved because it is associated with an increased risk of nephrotoxic effects. CKD stages (3–5) have been considered for determination of decrease in the estimated glomerular filtration rate (GFR) to be less than 60 mL/(min 1.73 m^2), while standards are 120–130 mL/(min 1.73 m^2) depending on the age, gender, and body size. Contrast agents have been recognized for their contrast-induced nephropathy (CIN). Therefore, contrast-enhanced imaging is considered one of the most challenging tasks in radiology on patients with severe renal inefficiency.

A major cause of critical kidney failure is renal toxicity of radio CM.[12,13] It was approved that nephrotoxicity is associated with use of contrast agents, especially in patients with risk factors. Ten Dam and Wetzels[14] have reported that iodinated CT contrast retains side effects; an increase in radiation ED was observed when comparing the enhancement of CT contrast in all organs studied pre- and post-injection of the contrast agent. Average dose increments were as follows: for the liver 19%, for the kidneys 71%, for the spleen and pancreas 33%, and for the thyroid 41%. Kidneys showed the maximum dose increment, whereas the pancreas exhibited the widest variance due to fibro-fatty involution. The dose increase from the change in attenuation was measured in Hounsfield units in comparison with an unenhanced CT scan.[15] One of the effects is CIN, which is correlated with CT, especially in patients who are at a high risk of nephrogenic systemic fibrosis.[1,14,16]

Despite the immediate benefits of CT examinations,[17] the relatively high radiation has raised health concerns because of the potential increase in cancer risk.[18] Since cancer risk is associated with the radiation dose, the ED typically measures the absorbed radiation dosage by means of ionized energy absorbed by irradiated organs. Thus, the measuring the radiation exposure helps assess risks of the diagnostic organ. Hence, this study represents two main areas. First, it scrutinizes the histotoxicity of CM *in vitro* by utilizing animal models as a means of administered intervention. The histotoxicity evaluations of the CM were performed utilizing local rabbits as a model to gain deeper insights into their behaviors. Additionally, animals receiving intravenous injections are examined post-injection to evaluate the impact of CM on renal function, with a particular focus on kidney function. The other aspect of this research involves examining the ED of CT scans for both native CT examinations and those involving CT CM. The CT ED was measured both with and without the CM to delineate its influence. Toxicity evaluation forms a significant aspect of this study, wherein blood samples are collected from various patients undergoing both native CT and CT with contrast examinations. Four parameters, namely, creatinine, creatinine clearance, blood urea, and GFR, are measured to assess the toxicity. These measurements are conducted utilizing the OTC11 system.

Materials and Methods

In vitro histotoxicity assay of computed tomography contrast media

A proficiently conducted study involved 14 local rabbits aged between 2 and 3 months, with weights (1300–1500) g. Before the experiment, these animals underwent a 3-day acclimatization period under controlled environmental conditions, maintaining a 12-h light/dark cycle. Throughout this period, all rabbits had unrestricted access to food and water.

Seven conscious and comfortably restrained white rabbits (designated as group A) were intravenously injected with isotonic saline at a dosage of 2 mL/kg.[19] The injection was manually administered into a marginal ear vein within a span of 60 s. Simultaneously, another seven rabbits (group B) received injections of 2 mL/kg of CT CM 350 I/mL.

Currently, water-soluble iodine CM are synthesized using triiodobenzoic acid by introducing iodine atoms on the aromatic ring. Iohexol is the most favorable CT clinical agent due to its benzene core with three iodine atoms for CT contrast and three amide and six alcohol groups, providing several physical properties such as sound attenuation, vascular imaging, and fast CT scanning enhancement.[3,20]

After 24 h post-injection of CT CM 350 I/mL; arterial blood samples were drawn from the marginal ear vein of all animals at the same time to measure blood urea and creatinine levels, indicating potential toxicity. Subsequently, the animals were euthanized, and kidney tissues were collected from both groups. These tissues were rinsed with a normal saline solution to remove surface blood. Following this, organs were immersed in a buffered paraformaldehyde solution for 24 h, dehydrated, and processed for paraffin embedding. Serial sections of 4-mm thickness were obtained and stained with hematoxylin and eosin. Histological examination of these sections under a microscope enabled the assessment of any histotoxic effects.

Measurements effective dose

The present study was conducted with proficiency at Al-Hussein Teaching Hospital in Samawah City, Al-Muthanna Governorate, Iraq. A cohort of 25 adult patients [17 male (68%) and eight female (32%)] was included from inpatient units and outpatient clinics. These patients underwent abdominal CT scans during 1- and 6-month follow-up examinations, employing a defined set of parameters. We used a 64-slice siemens CT scan, with

Table 1: Region-specific factor $K_{(age,gender)}$ values[21]

Region of body	Risk factor $K_{(age,gender)}$
Head	0.021
Abdomen	0.015
Chest	0.014

Table 2: Parameters of protocol

Parameters	Control head CT scan
Tube voltage (kVp)	120
Current (mA)	350
Pitch	0.6

CT: computed tomography

careful consideration given to specific organs coefficient of ages and gender [Table 1].

Ethical consent was obtained from the parents or relatives of all patients. Abdominal CT scans were conducted on patients aged between 15 and 70 years referred for CT examination due to various clinical indications. The ED measurement was provided by measuring the dose-length product of the CT scan, which was recorded from the CT dose report for each case.

CT examinations of native and contrast protocols were used for patients categorized based on gender and divided into three age groups (15–30 years, 31–44 years, and 45–70 years). The adjusted protocol parameters included potential voltage, tube current, and pitch, as presented in Table 2 to be a set of CT parameters used for the control protocols (native and contrast) to measure the ED for both native and contrast abdominal CT examinations.

Furthermore, ED was computed for each complementary pair of native and contrast protocols, enabling investigation into the effects of pre- and post-contrast Intravenous injections. A retrospective study proficiently incorporated measurements of ED for both unenhanced and contrast-enhanced abdominal CT scans using descriptive statistics.

Statistical analysis

In our study, the statistical analysis was performed to indicate the cytotoxicity effect of CM on the involved animals by measuring the urea and creatinine factors of the injected group with CM in comparison with the control group.

Then, we thoroughly assessed both native and contrast-enhanced abdominal CT examination findings. Each patient underwent a contrast-enhanced CT examination using 350 mg I/mL following unenhanced CT, employing identical scanning parameters and positioning with arms overhead. Toxicity was evaluated by obtaining blood samples for both native and contrast-enhanced CT examinations, focusing on four key parameters: creatinine, creatinine clearance, blood urea, and GFR, measured using the OTC11 system. Statistical analysis employed a completely randomized design with one-way analysis of variance and independent *t* tests at a 5% significance level to analyze ED data. Additionally, correlations between the ED values of native and contrast examinations were statistically examined using the Pearson correlation coefficient. Data processing and analysis were performed using the Statistical Package for the Social Sciences (SPSS) version 22 (SPSS, IBM Company, Chicago, IL USA), with results expressed as mean ± SD

Ethical approval

The study was approved by the local committee of Al-Muthanna University, College of Pharmacy, on June 18, 2024.

Results

In vitro histotoxicity evaluation

Compared to pre-injection, intravenously injected animals were used to evaluate the effects of the contrast agent on kidney function. In terms of renal function, the results indicate no deterioration. Compared to the control group, there was a slight increment in creatinine levels and a decline in urea levels in the CM group, as demonstrated in Table 3. Whereas the administrated iodine contrast agent dose (2 mL/kg) did not lead to any significant decline in kidney function.

Furthermore, a further investigation of whether CT CM can induce adverse effects such as (tissue damage, inflammation, or lesions) during the long-term post-injection involves performing a histopathological assessment of the rabbit's susceptible organs. A clear adverse effect associated with the administration of CT CM was observed compared to the control group.

Pathological findings of this study using H&E stain were noted in rabbit kidney tissue from the control group, which revealed a normal cortex and medullary region, as shown in Figure 1a and b.

In CM-treated rabbits, congested blood vessels, irregularities and degenerated renal glomerulus, necrosis of tubules, and proteinaceous casts were observed in the cortex region of the kidney [Figure 2a], whereas the observations of the medullary region of the kidney show detachment of tubule epithelium, degenerated collecting tubules, inflammatory cells, and eosinophilic fluid within the tubules, as illustrated in Figure 2b.

Analysis of the effective dose

CT examinations have greatly contributed to the diagnosis of many clinical diseases. However, radiation risks due to CT procedures are regarded as essential for the diagnosis

of patients. Therefore, the evaluation for native and contrast CT examination protocols represents the CT scan parameters according to Tables 1 and 2; the limited protocols represent the minimal standards that can be used for CT examination.

Abdomen CT scans performed with both (native and contrast) CT examinations were specifically examined for the diagnosis of adult patients; ED were measured, revealing no significant variations in distribution based on gender [$P = 0.891$ (native), $P = 0.888$ (contrast)] as mentioned in Table 4. Considering the direct irradiation that is required for CT procedures, protocols for native and contrast scans were evaluated to calculate ED for each procedure according to the gender [Table 4]. The analysis demonstrated no significant differences between native and contrast groups ($P > 0.05$).

On the other hand, for analysis of age, both protocols (native and contrast) were subdivided based on three age groups A strong distribution relationship was observed between the patient's age and ED ($P < 0.05$). The mean values of ED distribution varied notably among patients aged 15–30 years compared to other age groups, as illustrated in Table 5. The P value for ED in the native protocol was 0.000, and similarly, the P value for ED in the contrast protocol was also 0.000, which indicated a statistically significant difference between native and contrast parameters, especially for patients aged 15–30 years old (age group 3). However, there was no significant difference for the other age groups (age group 1 and age group 2).

Consequently, comparisons of overall disruptions of ED values between native and contrast protocols showed there are no significant differences in ED means ± SD for the native was 9.65 ± 4.9, while it was 9.69 ± 4.94 for the contrast protocol [Table 6].

Table 3: Comparison of animal blood parameters between control and treated groups with computed tomography contrast groups

Treatments	Parameters	
	Creatinine mg/dL mean ± SD	Urea mg/dL mean ± SD
Control group	0.97 ± 0.13	54.01 ± 6.51
Contrast group	0.98 ± 0.11	38.56 ± 4.21

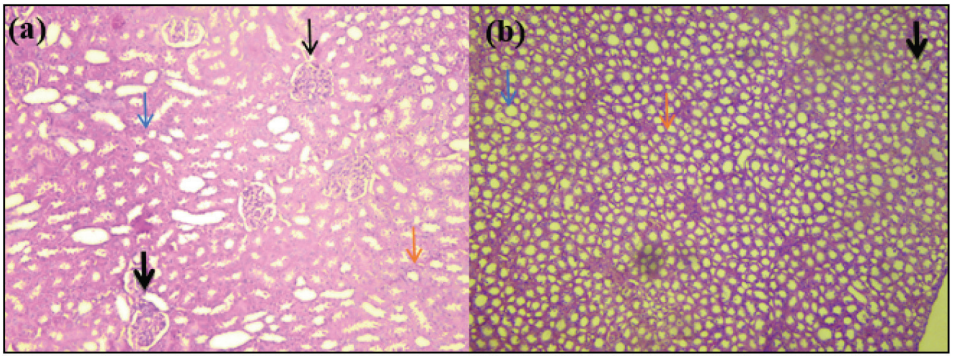

Figure 1: (a) Section from the control rabbit cortex region of the kidney showing the following: normal renal corpuscle with glomeruli (black arrow), normal proximal convoluted tubules (blue arrow), and normal distal convoluted tubules (red arrow) (H&E 10×). (b) Section from the control rabbit medulla region of kidney showing: normal descending tubules (black arrow), normal ascending tubules (blue arrow), and normal collecting tubules (red arrow) (H&E 10×)

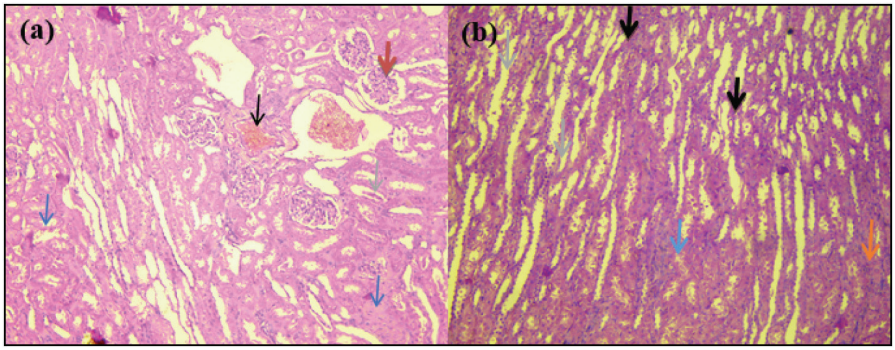

Figure 2: (a) Section from the cortex region of kidneys of rabbits treated with a contrast media (CM) showing: congested of blood vessels (black arrow), irregularities and degenerated renal glomerulus (red arrow), and necrosis of tubular (blue arrow) proteinaceous casts (green arrow) at magnification 10×. (b) Section from the medullary region of kidney of rabbits treated with a CM showing: detachment of tubules epithelium (black arrow), degenerated collecting tubules (green arrow), inflammatory cells (blue arrow), and eosinophilic fluid in tubules (red arrow) (H&E 10×)

Table 4: Distribution of native and contrast groups of effective dose means according to gender (female and male)

Sex	Native mean ± SD	Contrast mean ± SD
Female	9.48 ± 5.4	9.5 ± 5.5
Male	9.7 ± 4.7	9.8 ± 4.7
P value	0.891	0.888

[a]Significant difference at $P \leq 0.05$

Table 5: Distribution of native and contrast groups of effective dose means according to age groups

Age	Native mean ± SD	Contrast mean ± SD
Age group 1	5.5 ± 0.83	5.57 ± 0.81
Age group 2	7.6 ± 2.6	7.6 ± 2.69
Age group 3	15.1 ± 3.45	15.19 ± 3.43
P value	0.000*	0.000*

*Significant difference at $P \leq 0.05$

Table 6: Comparison of effective dose means between native and contrast groups among patients' abdomen samples

Parameters	Native mean ± SD	Contrast mean ± SD	*P* value
ED	9.65 ± 4.9	9.69 ± 4.9	0.973

[a]Significant difference at $P \leq 0.05$

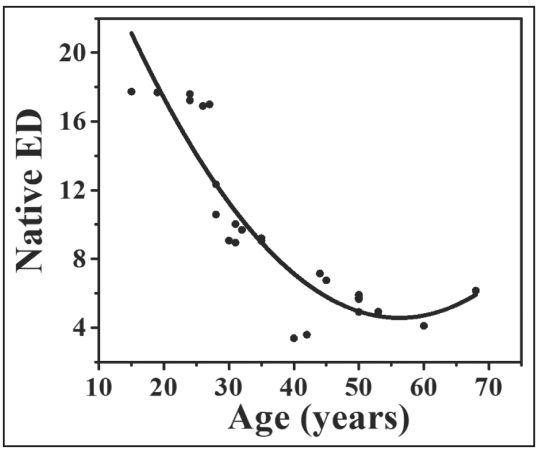

Figure 3: The relation between the age and effective dose of native computed tomography scan

Furthermore, the relation between the EDs of a native CT scan with respect to patients' age is assessed. It was shown that ED is increased with a decrease in the patient's age. The highest ED is recorded with the youngest patient's age at 15 years, as represented in Figure 3.

Likewise, a robust correlation was identified between age and CT examination with CM. The youngest age group exhibited the highest absorption of dose, as shown in Figure 4.

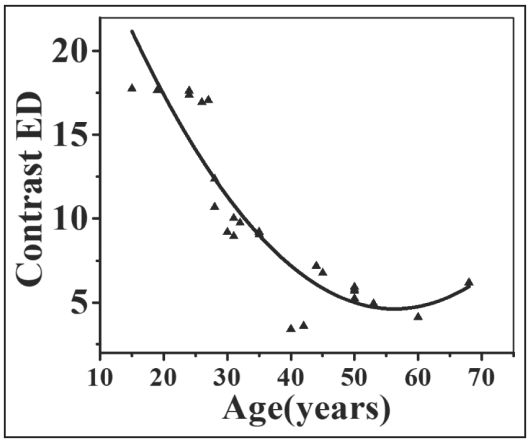

Figure 4: The relation between the age and effective dose of computed tomography with contrast media

Table 7: Comparison of blood parameters between native and contrast groups among patients' abdomen samples

Parameters	Native mean ± SD	Contrast mean ± SD	*P* value
Urea	15.6 ± 4.8	17 ± 4.1	0.418
Creatinine	0.880 ± 0.2	0.886 ± 0.19	0.927
GFR	104.2 ± 22.1	104.2 ± 22.1	1.000
CrCl	109.06 ± 19.31	109.08 ± 19.32	0.999

GFR: glomerular filtration rate.
[a]Significant difference at $P \leq 0.05$

In vitro toxicity assay of computed tomography contrast agent

Nephrotoxicity is associated with the use of an iodine contrast agent, which is considered as a risk factor of renal failure. CT protocols have been significantly used for clinical diagnosis for anatomical and physiological (CE-CT) imaging, which requires intravenous administration of CM. Injection of iodinated CT CM may cause CIN in some cases, leading to iatrogenic acute renal failure. Patients with CKD (stage 3–5) are at major risk for development of CIN. Therefore, nonionic low osmolality contrast media, hydration, and a minimum volume of contrast agent should be used. It would be important to precisely compare the risk–benefit ratio of contrast-enhanced CT in patients by measuring the indicated parameters of toxicity (creatinine, creatinine clearance, blood urea, and GFR).

Four factors of blood samples were measured in this study to indicate the toxicity. It was found that there is no significant difference because of the CM. The *P* value for the blood urea parameter is 0.418, the creatinine *P* value is 0.927, GFR is 1.000, and creatinine clearance is 0.999, as presented in Table 7.

Discussion

Histotoxicity evaluation

It is essential to evaluate the histotoxicity effects of CM by conducting experiments on local rabbits as a model

to further confirm the behavior of CM. Table 3 does not shown any significant decline in kidney function. This is because CM can reduce blood flow though the kidney and cause hypoxic damage, that is, the outer medulla. In addition, reduction of tubular fluid is similarly affected because of CM, which was compatible with previously reported results.[19,22] These results were in line with those of Walday *et al*.[23] who found that the injected CT CM doses up to 10.5 g I/kg in rabbits did not have significant effects on urea and creatinine levels. In contrast to this study, Avades[22] has reported that CM can cause acute kidney injury by different mechanisms including vasoconstriction of the renal vasculature, increasing in the oxidative stress level, and altering renal protein transport and metabolism. Mamoulakis *et al.*[24] evaluated novel biomarkers of nephrotoxicity in blood and tissue samples of CIN in animal models. Serum creatinine (sCr) and symmetric-asymmetric dimethylarginine (SDMA-ADMA) levels indicated developed CIN. The results showed a 68.2% increase in mean sCr levels within 48 h with a significant elevation in SDMA-ADMA levels at 0 and 24 h, with a slight decrease at 48 h, while the control group remained normal at all time points.[24] Koo *et al.*[25] examined the effects of repetitive administration of IV iodinated CM on the long-term renal function of patients with early-phase gastric cancer. This study indicated that repetitive administration of IV iodinated contrast may result in a decline in renal function over time in these patients. This finding highlights the significance of studying the cumulative effects of repetitive administration of IV iodinated CM on renal function.[25]

Our observations of histopathological lesions related to CM [Figure 2a and b] were in line with those of other studies, such as Yang *et al*.[26] and Yao *et al*.[27] who mentioned that CT CM could directly affect renal tissue. Irregularities in renal glomerular occur after CMN which is in agreement with Asy'ari *et al.*[28] who observed both tubular necrosis and protein casts in renal tissue after intravascular injection of iodinated CM (iohexol) and (iopamidol) in male Wistar strain white rats. The other study done by Andreucci *et al*.[29] reported radio CM (RCM) that are medical drugs, which were used to improve the visibility of internal organs and structures in X-ray-based imaging techniques, may have side effects ranging from itching to life-threatening emergency, known as CIN as acute renal failure occurring within 24–72 h of exposure to RCM that cannot be attributed to other causes.[29] It usually occurs in patients with preexisting renal impairment and diabetes. The mechanisms underlying CIN include a reduction in medullary blood flow leading to hypoxia and direct tubule cell damage and the formation of reactive oxygen species.

The most important histopathological lesion of acute nephrotoxicity is necrosis, especially in proximal convoluted tubules; the prevalence of necrotic phenomena in rats with CIN has been previously reported.[30-32] The generalized necrosis present in rabbits in this study is in agreement with the previously reported study.[33] Proximal convoluted tubules are more prone to necrosis following xenobiotic administration than medullary collecting ducts or distal convoluted tubules. The proximal tubular epithelium is the kidney region where most of the membrane-bound active transport activity occurs. It has increased permeability to ions and chemical influx than the distal tubular epithelium, due to higher electrical resistance and tighter intracellular junctions.[34] In addition, proximal tubules are more susceptible to ischemic and toxic injury. This is due to a consequence of their lower capacity for anaerobic glycolytic ATP production and lack of antioxidant in addition to antiapoptotic proteins. The higher electrical resistance and tighter intracellular junctions are also found as proteinaceous casts in medullary tubular ducts, mostly in the inner zone of the medullary region, while this result disagrees with our study. However, proteinaceous casts in the kidneys indicate an important role of intranephronal obstruction in the pathogenesis of renal failure and increased proximal tubule pressures and simultaneously reduced single nephron GFR with intravenous infusion.

Effective dose

The results reflected a higher risk coefficient, which means an increase in the radiation dose because of CM[15] according to the following equation.

$$\mathrm{ED} = K\left(\text{gender, age}\right) \times \mathrm{DLP} \tag{1}$$

Therefore, the result shows no significant variations in distribution based on gender, as mentioned in Table 4;[13] this finding is consistent with that of Pearce *et al*.[18] However, the outcomes clarified in Table 5 indicated that ED was strongly dependent on the patient's age; this finding is consistent with that of Brenner *et al*.,[35] who showed robust differences according to age. Furthermore, the correlation between age and CT examinations was identified as follows: the youngest age group exhibited the highest absorption of dose.

Toxicity assay

Toxicity effect of CT radiation is considered a risk factor of renal failure,[14,36] CT CM on blood samples is presented in Table 7. Blood urea is one of the factors that could be used to indicate the increase of iohexol toxicity in blood. It helps observe how well the kidneys are working. In general, around 7–20 mg/dL (2.5–7.1 mmol/L) is considered normal, so a higher level than normal range indicates kidney injury or disease. Iohexol is one of many medicines that may cause a high B-urea level, this finding was compatible with that of [37].

A creatinine clearance test measures how well creatinine is removed from the blood by kidneys. The test is done on

both a blood sample and on a sample of urine collected over 24 h. It can be estimated by a formula using serum (blood) creatinine level, patient's weight, and age.[38]

$$\mathrm{CrCl(male)} = \left[(140 - \mathrm{age})\,\mathrm{BW}\right] / 72 \times \mathrm{Scr}, \quad (2)$$

$$\mathrm{CrCl\ (female)} = \left[0.85(140 - \mathrm{age})\,\mathrm{BW}\right] / 72 \times \mathrm{Scr}. \quad (3)$$

Estimated GFR is the best test to measure levels of kidney function and determine the stage of kidney disease.[13] It can be calculated from the results of the blood creatinine test, age, body size, and gender. GFR identifies the stage of kidney disease and helps with treatment. If the GFR number is low, kidneys are not working as well as they should.

So iohexol, a nonionic contrast agent, is most suited to replace inulin as the marker of choice for GFR determination. Iohexol comes very close to fulfilling all requirements for an ideal GFR marker in terms of low extra-renal excretion, low protein binding, and in being neither secreted nor reabsorbed by the kidney. In addition, iohexol is virtually nontoxic. As iohexol is stable in plasma, administration, and sample analysis can be separated in both space and time, allowing access to GFR determination across different settings.[39]

Conclusion

This study underscores significant concerns regarding CM usage in CT imaging. Our research provides thorough evaluations of both histotoxicity and ED measurements. Our study critically assessed renal function in animals following intravenous injection of CM, and further investigation of whether CT CM can induce adverse effects is required. This involved performing histopathological assessment of clear adverse effects associated with the administration of CT CM. Furthermore, a notable correlation between patient age and ED in CT examinations was observed among human subjects. CT ED is significantly impacted is higher risks on young patients; however, no substantial influence was observed related to the gender of patients. These findings emphasize the necessity of carefully balancing diagnostic efficacy benefits with potential risks associated with contrast-enhanced CT imaging. Optimizing protocols is crucial to minimize radiation exposure while ensuring diagnostic accuracy and patient safety.

Acknowledgement

The authors of this paper express their gratitude to the Iraq Ministry of Higher Education and Scientific Research, College of Pharmacy at Al-Muthanna University, as well as to the administration of Al-Hussein Teaching Hospital in Al-Samawa city, Iraq for their proficient technical support.

Authors contributions

All author are equally contributed.

Data availability statement

All data are available at request.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Hasebroock KM, Serkova NJ. Toxicity of MRI and CT contrast agents. Expert Opin Drug Metab Toxicol 2009;5:403-16.
2. Lusic H, Grinstaff MW. X-ray-computed tomography contrast agents. Chem Rev 2013;113:1641-66.
3. Koç MM, Aslan N, Kao AP, Barber AH. Evaluation of X-ray tomography contrast agents: A review of production, protocols, and biological applications. Microsc Res Tech 2019;82:812-48.
4. Faraj KA. Ionizing radiation-induced non-cancer diseases. Med J Babylon 2023;20:228-35.
5. Hallouard F, Anton N, Choquet P, Constantinesco A, Vandamme T. Iodinated blood pool contrast media for preclinical X-ray imaging applications - A review. Biomaterials 2010;31:6249-68.
6. Yeh BM, FitzGerald PF, Edic PM, Lambert JW, Colborn RE, Marino ME, *et al*. Opportunities for new CT contrast agents to maximize the diagnostic potential of emerging spectral CT technologies. Adv Drug Deliv Rev 2017;113:201-22.
7. Fang Y, Peng C, Guo R, Zheng L, Qin J, Zhou B, *et al*. Dendrimer-stabilized bismuth sulfide nanoparticles: Synthesis, characterization, and potential computed tomography imaging applications. Analyst 2013;138:3172-80.
8. Hainfeld JF, Slatkin DN, Focella TM, Smilowitz HM. Gold nanoparticles: A new X-ray contrast agent. Br J Radiol 2006;79:248-53.
9. Zhang M, Ju H, Zhang L, Sun M, Zhou Z, Dai Z, *et al*. Engineering iodine-doped carbon dots as dual-modal probes for fluorescence and X-ray CT imaging. Int J Nanomed 2015;10:6943-53.
10. Lönnemark M, Magnusson A, Ahlström H. Oral contrast media in CT of the abdomen. Acta Radiol 1993;34:517-9.
11. Talmon A, Tal Y, Moss J, Hershkowitz I, Shaham D, Sosna J, *et al*. Clinical impact of allergy and pre-medication in CT studies with low-osmolality intravenous iodinated contrast media. Clin Radiol 2022;77:210-5.
12. Faucon AL, Bobrie G, Clément O. Nephrotoxicity of iodinated contrast media: From pathophysiology to prevention strategies. Eur J Radiol 2019;116:231-41.
13. Andreucci M, Faga T, Pisani A, Sabbatini M, Michael A. Acute kidney injury by radiographic contrast media: Pathogenesis and prevention. Biomed Res Int 2014;2014:362725.
14. ten Dam MAGJ, Wetzels JFM. Toxicity of contrast media: An update. Neth J Med 2008;66:416-22.
15. Amato E, Salamone I, Naso S, Bottari A, Gaeta M, Blandino A. Can contrast media increase organ doses in ct examinations? A clinical study. AJR Am J Roentgenol 2013;200:1288-93.
16. Fadhel AA, Yousif AK. Correlation of glycated hemoglobin (Hba1c) and serum uric acid in type-2 diabetic patients. Indian J Public Health Res Dev 2019;10:1250-4.
17. Herts BR, Baker ME, Obuchowski N, Primak A, Schneider E, Rhana H, *et al*. Dose reduction for abdominal and pelvic MDCT after change to graduated weight-based protocol for selecting quality reference tube current, peak kilovoltage, and slice collimation. AJR Am J Roentgenol 2013;200:1298-303.
18. Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, *et al*. Radiation exposure from CT scans in childhood and subsequent

risk of leukaemia and brain tumours: A retrospective cohort study. Lancet 2012;380:499-505.
19. Kirberger RM, Cassel N, Carstens A, Goddard A. The effects of repeated intravenous iohexol administration on renal function in healthy beagles--A preliminary report. Acta Vet Scand 2012;54:47.
20. He W, Ai K, Lu L. Nanoparticulate X-ray CT contrast agents. Sci China Chem 2015;58:753-60.
21. Sarangi PK, Mohanty J, Parida S, Swain BM. Understanding computed tomography (CT) dose reduction techniques and principles in a simplified way. Curr Trends Clin Med Imaging 2017;1:1-6.
22. Avades T. Renal Effects of X-ray Contrast Media in Different Experimental Models. Guildford: University of Surrey; 1997.
23. Walday P, Heglund IF, Golman K, Cornacoff J, Holtz E. Renal effects of iodixanol in experimental animals. Acta Radiol Suppl 1995;399:204-12.
24. Mamoulakis C, Fragkiadoulaki I, Karkala P, Georgiadis G, Zisis IE, Stivaktakis P, *et al*. Contrast-induced nephropathy in an animal model: Evaluation of novel biomarkers in blood and tissue samples. Toxicol Rep 2019;6:395-400.
25. Koo JH, Lee M, Kim EH, Oh HJ, Lim JS, Hyung WJ, *et al*. Harmful effect of repetitive intravenous iodinated contrast media administration on the long-term renal function of patients with early gastric cancer. Sci Rep 2023;13:1-9.
26. Yang JS, Peng YR, Tsai SC, Tyan YS, Lu CC, Chiu HY, *et al*. The molecular mechanism of contrast-induced nephropathy (CIN) and its link to in vitro studies on iodinated contrast media (CM). BioMedicine 2018;8:1-11.
27. Yao L, Kolluru GK, Kevil CG, Zhang WW. Intravascular radiocontrast iodixanol increases permeability of proximal tubule epithelium: A possible mechanism of contrast-induced nephropathy. Vasc Endovascular Surg 2013;47:632-8.
28. Asy'ari AH, Rahaju AS, Mustika A. Histopathology and renal function in wistar rats after intravascular injection of iodinated contrast media iohexol and iopamidol. Syntax Lit J Ilm Indones 2022;7:362-70.
29. Andreucci M, Solomon R, Tasanarong A. Side effects of radiographic contrast media: Pathogenesis, risk factors, and prevention. Biomed Res Int 2014;2014:1-20.
30. Ari E, Kedrah AE, Alahdab Y, Bulut G, Eren Z, Baytekin O, *et al*. Antioxidant and renoprotective effects of paricalcitol on experimental contrast-induced nephropathy model. Br J Radiol 2012;85:1038-43.
31. Buyuklu M, Kandemir FM, Ozkaraca M, Set T, Bakirci EM, Topal E, *et al*. Benefical effects of lycopene against contrast medium-induced oxidative stress, inflammation, autophagy, and apoptosis in rat kidney. Hum Exp Toxicol 2015;34:487-96.
32. Ozkan G, Ulusoy S, Orem A, Ersoz S, Alkanat M, Yucesan FB, *et al*. Protective effect of the grape seed proanthocyanidin extract in a rat model of contrast-induced nephropathy. Kidney Blood Press Res 2013;35:445-53.
33. Lauver DA, Carey EG, Bergin IL, Lucchesi BR, Gurm HS. Sildenafil citrate for prophylaxis of nephropathy in an animal model of contrast-induced acute kidney injury. PLoS One 2014;9:1-15.
34. Sahota PS, Popp JA, Hardisty JF, Gopinath C. Toxicologic Pathology: Nonclinical Safety Assessment. Boca Raton: CRC Press; 2013. p. 1015.
35. Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric CT. Am J Roentgenol 2001;176:289-96.
36. Assi MH, Zghair MA, Ghanem M. Computed tomographic assessment of renal length in correlation to anthropometric parameters: A cross-sectional hospital-based observational study from Iraq. Med J Babylon 2023;20:808-16.
37. Uchino S, Bellomo R, Goldsmith D, Journal CK. The meaning of the blood urea nitrogen/creatinine ratio in acute kidney injury discussion key findings. Clin Kidney J 2012;74:187-91.
38. Lascelles PT, Donaldson D. Creatinine clearance test. In: Diagnostic Function Tests in Chemical Pathology. 1st ed., Dordrecht: Springer, 1989. p. 33-4.
39. Delanaye P, Ebert N, Melsom T, Gaspari F, Mariat C, Cavalier E, *et al*. Iohexol plasma clearance for measuring glomerular filtration rate in clinical practice and research: A review. Part 1: How to measure glomerular filtration rate with iohexol? Clin Kidney J 2016;9:682-99.