

Incidence of Acute Kidney Injury due to Contrast Usage in Patients Admitted to Mofid Children's Hospital (2019-2020)

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Abstract

Background and aims: Contrast-induced renal impairment endangers the patients' health and imposes a financial burden on families and the health care system. Therefore, this study was conducted to examine the rate of nephropathy in patients admitted to Mofid Children's Hospital in 2018 and 2019.

Methods: In this cross-sectional study serum creatinine was measured at baseline and 48-72 hours after CT-scan an increase of more than 25% in serum creatinine was considered CIN. Paired sample t-test was used to assess the change in the Cr. The research data were analyzed using SPSS-25 software and the significance level in all tests was set at $P = 0.001$.

Results: In this study, 180 children underwent contrast-enhanced CT-scan with a mean age of 5.72 years, of whom 81 (45%) were girls and 99 (55%) were boys. The mean baseline creatinine was 0.633 ± 0.137 mg / dl, which increased significantly to 0.675 ± 0.164 mg / dl 48-72 hours after the first measurement. The chance of developing ARF in ciprofloxacin users was 4.86 times higher than patients who did not use this drug.

Conclusion: In children underwent CT scan, the incidence of ARF is 17.2%. Ciprofloxacin increases the risk of acute kidney problems by 4.8 times.

Keywords: Acute Kidney Injury; Contrast Nephropathy; Ciprofloxacin; Child.

Conflict of interest: The authors declare no conflict of interest.

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Introduction

Acute renal failure (ARF) is one of the major public health problems worldwide causing more than one million kidney transplants. In the last decade, the term acute renal failure (ARF) was used, although it is now known as acute kidney injury (AKI) because acute kidney injury must be detected in the early phase to prevent failure (1). Contrast induced-nephropathy (CIN) is a very common and preventable cause of acute renal failure.

It is a complication of intravenous arteriography and CT scan and is considered the third most common cause of acute renal failure in hospitalized patients (2). Renal impairment due to contrast media (CM) is usually defined as an increase of 25% or more in the serum creatinine level relative to baseline or an absolute increase in serum creatinine level of at least 0.5 mg/dL resulting from the use of contrast media (3). Acute renal failure usually occurs in the form of

an asymptomatic increase in creatinine and is mainly non-oliguric. The maximum increase in the creatinine level is on the third to fifth day and usually resolves within 10 to 14 days, but oliguric acute kidney injury occurs in some cases. In these patients, the creatinine level peaks between the fifth and tenth days and returns to baseline within 2 to 3 weeks. It seems that contrast-induced renal disorders result from a potentiating effect of renal circulation changes along with decreased blood flow and direct intoxication of the central renal medulla (4-5).

Diabetes, chronic kidney failure, severe congestive heart failure, fluid loss (dehydration), and hypotension are risk factors for acute tubular necrosis due to contrast agents. The type and volume of contrast media are also important factors in damage to renal tubules (6). The rate of contrast-induced nephropathy increases to 43% in patients with diabetes and 50-90% in chronic renal failure patients. If renal failure due to contrast-induced nephropathy leads to dialysis, the prognosis is severely impaired, with 36% of patients dying in the hospital and a 2-year life expectancy of about 19% (7). The three main factors involved in the pathogenesis of substance-induced nephropathy are 1. Direct nephrotoxicity of iodinated contrast media: direct toxicity of contrast media on nephrons seems to be directly related to the degree of ionization of the contrast media and its osmolality, 2. Small kidney thromboembolism: cholesterol embolism appears in about 50% of angiography cases in which the guiding catheter is inserted into the aorta. Many of these emboli are asymptomatic. 3. Intrarenal vasoconstriction: this will lead to worsening of hypoxia (8).

The incidence of CIN is highly variable and ranges from 0% to 50%. This variation is due to differences in the presence or absence of risk factors (especially chronic kidney disease), the amount and type of contrast used, CIN definition, prospective or retrospective design of the study, determination of incidence, and the radiological process performed. The incidence of CIN in individuals with baseline mild-to-moderate renal insufficiency (creatinine 1.5-4 mg/dl) is 4-11%. This risk may be exacerbated by severe renal impairment, significant volume loss, severe heart failure, or multiple contrast-enhanced radiographic studies over 72 hours. The incidence of CIN in patients with mild-to-moderate renal insufficiency and diabetes is between 9% and 38%.

The incidence of CIN is 50% or more if baseline plasma creatinine exceeds 5-4 mg/dl, especially in the presence of diabetic nephropathy (9-11). Due to the high incidence of this injury and its risk in patients, especially children, and considering the direct effects of this disease on the length of hospital stay, the general condition of the patient, and the cost imposed on the health economics, it is crucial to investigate the incidence of this complication in patients. Therefore, this study was conducted to investigate the incidence of acute renal failure due to contrast nephropathy in patients admitted to Mofid Children's Hospital during 2018 and 2019. The results can be used to improve patient care.

Methods

This cross-sectional study was conducted on 180 children that underwent contrast-enhanced CT scan in Mofid Children's Hospital during 2018 and 2019. Using the information in the patients' electronic files, the required demographic information such as age, sex, race, and weight as well as clinical information such as underlying disease, reason for CT-scan, type and volume of contrast media, comorbidities including heart failure, chronic renal failure, history of glomerulonephritis, and use of nephrotoxic substances were identified. History of hospitalization was also inquired. Serum creatinine (bCr) was measured at baseline and 48-72 hours after contrast-enhanced CT scan. CIN was considered if there was an increase of more than 25% in serum creatinine. Other risk factors such as bleeding, sepsis, mechanical ventilation or administration of vasodilators were also determined.

Statistical analysis methods

Quantitative data are presented as mean and standard deviation and qualitative data are reported as frequency and percentage. Paired sample t-test was used to assess the change in the Cr. The Shapiro-Wilk test was used to evaluate the normality of quantitative data distribution. Independent t-test, Mann-Whitney, and Chi-square (if necessary, Fisher's exact test) were used to compare the characteristics between the two groups of patients. Logistic regression was used to investigate the relationship between each variable and the incidence of ARF. The significance level for all tests was set at 0.05. SPSS software version 25 was used for data analysis.

Results

In this study, 180 children that underwent contrast-enhanced CT scan were evaluated. The mean age of the children was 5.72 ± 3.87 years ranging from 1 month to 15 years and 9 months. Furthermore, 81 patients (45%) were girls and 99 (55%) were boys. The mean baseline creatinine was 0.633 ± 0.137 mg/dl, which significantly increased to 0.675 ± 0.164 mg/dl 48-72 hours after the first measurement ($p = 0.001$). Renal impairment was determined based on an absolute increase of 0.5 mg / dL relative to baseline creatinine or an increase of 25% or more in serum creatinine relative to baseline. Accordingly, 31 patients (17.2%) had ARF. Thus, the patients were divided into two groups of ARF ($n = 31$) and control group ($n = 149$).

The male to female ratio was 13 to 18 in the ARF 86.63 in the control group. There was no significant difference in the sex ratio between the ARF and control group ($p = 0.108$). In addition, the chance of developing ARF was 47% lower in males than in females, which was not statistically significant (OR = 0.529; 95% CI (0 - 1.16)). The mean age of the patients in the ARF and control group was 5.74 ± 4.21 and 5.72 ± 3.87 years respectively, indicating no significant difference between the two groups ($p = 0.982$). There was no statistically significant relationship between the age and ARF (OR = 1.001; 95% CI: 0.907 - 1.11; $p = 0.982$).

One hundred and one patients (1.56%) used at least one nephrotoxic drug. Twenty patients in the ARF group (71%) and 79 patients in the control group (53%) used nephrotoxic drugs.

Although the use of nephrotoxic drugs was higher in patients with ARF, no statistically significant relationship was observed between the use of nephrotoxic drugs and ARF (OR = 2.17; 95% CI: 0.935 - 5.02; $p = 0.0670$). There was no significant difference in the proportion of patients taking NSAIDs ($p = 0.144$), cisplatin ($p = 0.130$), vancomycin ($p = 0.116$), aminoglycosides ($p = 0.176$), and cyclophosphamide ($p = 0.057$) between the two groups.

The proportion of ciprofloxacin users was higher in the ARF group (5.4 vs. 16.1, $p = 0.042$). In addition, the risk of ARF (odds ratio) was 4.86 times higher in ciprofloxacin users compared to patients who did not take this drug (OR = 4.86; 95% CI: 1.31 - 18.11; $p = 0.018$).

Thirty-five patients (4.19%) had comorbidities, including 6 patients in the ARF group (19.4%) and

29 patients (5.19%) in the control group. There was no statistically significant relationship between comorbidity and acute kidney disease (OR = 0.993; 95% CI: 0.373 - 2.64; $p = 0.989$). About 13% of the patients in the ARF group and 9.4% of the patients in the control group were connected to a mechanical ventilator, but there was no statistically significant difference between the two groups ($p = 0.708$). Vasopressor was observed in 12.9% of patients with ARF and 10.7% of the control group but the difference was not significant between the two groups ($p = 0.881$). Sepsis was found in 9.7% of the patients in the ARF group and 8.1% of the patients in the control group, indicating no statistically significant difference between the two groups ($p = 0.999$).

The mean baseline glomerular filtration rate (GFR) was 103 ± 27.28 in the control group and 88.93 ± 23.88 in patients with ARF (Table 1).

Table 1. Effect of baseline GFR on acute renal failure (ARF)

Study group	Mean	SD	P-value	OR (95%CI)
ARF	88.93	23.88	0.004	1.02(1.01-1.04)
Control	103	27.28		

Most of the patients were hospitalized in the internal medicine ward (6.75%), including 83.9% of the patients in the ARF group and 73.8% of the patients in the control group. In addition, 9.7% of the patients in the ARF group and 11.4% of the patients in the control group were hospitalized in the intensive care unit (ICU). There was no statistically significant relationship between in-patient wards and ARF ($p = 0.425$).

Surgery, malformation, surgical evaluation, and other indications for CT scan were observed in 12.9%, 3.2%, 74.2%, and 9.7% of the patients in the ARF group and 21.5%, 5.4%, 52.3%, and 20.8% of the patients in the control group, respectively. There was no statistically significant relationship between CT scan indication and ARF incidence in patients ($p = 0.168$).

Thirty-day mortality was observed in 9.7% of patients with ARF and 13.4% of the control group. Thirty-day hospitalization in the ICU was observed in 12.9% of the patients with ARF and 10.1% of the patients in the control group.

Other 30-day outcomes were observed in 77.4% of the patients with ARF and 75.6% of the patients in the control group.

Model I shows that use of ciprofloxacin (OR = 4.86; $p = 0.018$) increased the risk of ARF (odds ratio) by 4.8 times. Adjusting for the effect of age

and sex showed that the risk (odds ratio) of ARF was 4.36 times higher in ciprofloxacin users compared to patients that did not use nephrotoxic drugs (OR = 4.36; $p = 0.030$) (Table 2).

Table 2. Results of regression model for the effect of influencing factors on the incidence of ARF

Model I			Model II		
Odds ratio	95% confidence interval for the odds ratio	P-value	Odds ratio	95% confidence interval for the odds ratio	P-value
Not taking nephrotoxic drugs					
Taking ciprofloxacin	1.31-18.11	0.018	4.36	1.15-16.51	0.030
	4.86				
Taking other nephrotoxic drugs					
	0.788-4.46	0.163		0.731-4.30	0.205
	1.86		1.77		
Model I: Unadjusted model					
Model II: Adjusted model for age and sex					

Discussion

In this study, 180 children who underwent contrast-enhanced CT-scan were studied. The mean age of the children was 5.72 years. The youngest child was one month old and the oldest was 15 years and 9 months old. As for the sex composition, 81 children (45%) were female and 99 (55%) were male. The mean baseline creatinine was 0.633 ± 0.137 mg/dl, which increased significantly to 0.675 ± 0.164 mg/dl 48-72 hours after the first measurement. Thirty-one patients (17.2%) developed ARF. Mitchell et al. found that 11% of the patients developed CIN, which is consistent with the results of the present study. However, the discrepancy in some results may be due to the larger sample size of the above study (633 subjects) (12).

The male to female ratio was 13 to 18 in patients with AFR and 86.63 in the control group, indicating no statistically significant difference in the sex ratio between the two groups. In addition, the chance of developing ARF was 47% lower in males compared to females, which was not statistically significant. The mean age of the patients in the ARF and control groups was 5.4 ± 74.21 and 5.72 ± 3.87 years respectively, indicating no statistically significant difference between the two groups. In a study by Lakovou et al., it was found that age and sex were

effective factors in the CIN, and sex was effective in mortality, which was different from the results of the present study. This difference may be due to the type of underlying disease and the older age of the patients compared to the present study (13).

One hundred and one patients (56.1%) took at least one nephrotoxic drug. Twenty-two patients in the ARF group (71%) and 79 patients in the control group (53%) took nephrotoxic drugs. Although the use of nephrotoxic drugs was higher in patients with ARF, no statistically significant relationship was found between the use of nephrotoxic drugs and ARF. The proportion of patients taking NSAIDs, cisplatin, vancomycin, aminoglycosides, and cyclophosphamide was not significantly different between the two groups. The proportion of ciprofloxacin users was higher in patients with ARF versus other patients (5.4 % vs. 16.1%; $p=0.042$). In addition, the chance of developing ARF was 4.86 times higher in ciprofloxacin users compared to patients who did not use this drug ($p = 0.018$).

Surgery, malformation, surgical evaluation, and other indications for CT scan were observed in 12.9%, 3.2%, 74.2%, and 9.7% of the patients in the ARF group and 21.5%, 5.4%, 52.3%, and 20.8% of the patients in the control group respectively, indicating no statistically significant relationship

between CT scan indication and the incidence of ARF ($p = 0.168$).

Most of the patients were hospitalized in the internal medicine ward (6.75%), including 83.9% of the patients with ARF and 73.8% of the patients in the control group. In addition, 9.7% of the patients with ARF and 11.4% of the patients in the control group were hospitalized in the intensive care unit. There was no significant relationship between the in-patient ward and ARF.

Thirty-day mortality was seen in 7.9% of the patients with ARF and 13.4% of the patients in the control group. Thirty-day hospitalization in the ICU was observed in 12.9% of the patients with ARF and 10.1% of the patients in the control group. Other 30-day outcomes were observed in 77.4% of the patients in the ARF and 75.6% of the patients in the control group. There was no significant relationship between 30-day outcomes and ARF. In a study by Mitchell et al., the authors found that of 1% of the patients ($n=7$) that had severe renal failure mostly caused by CIN, four died. This study found that CIN was followed by chronic and severe renal failure, which is different from the current study results (12).

Conclusion

The incidence of ARF was 17.2% in children that underwent contrast-enhanced CT scan. Age and sex did not affect the incidence of CIN. Comorbidities, mechanical ventilator use, vasopressor use, and sepsis in were not associated with CIN patients undergoing contrast-enhanced CT scan. CIN and ARF had no significant relationship with CT scan contraindications, surgery, malformation, 30-day mortality, ward hospitalization, and ICU hospitalization. Ciprofloxacin use was associated with a 2-fold increase in the risk of ARF development.

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Conflict of Interest

The authors declare no conflict of interest.

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Ethics

This study was approved by Ethics and Research Committee of Shahid Beheshti Medical University (IR. SBMU.MCP.REC.1398.588).

Authors Contributions

Methodology and Formal Analysis, Dr. Armin Shirvani; Writing Original Draft Preparation, Dr. Zohreh Nickhoo; Writing Review and Editing, Dr. Nasrin Esfandiar, Dr. Mitra Khalili and Dr. Reza Dalirani.

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