

# Routine Screening of Renal Function Before Intravenous Contrast Examination: Is this Required in the Indian Scenario?

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## Abstract

**Background:** Serum creatinine (SC) levels are routinely obtained before administering intravenous contrast agents to assess the risk of developing contrast-induced nephropathy (CIN). We reviewed the renal profile of Indian patients attending our department to assess if SC levels are routinely required and the importance of calculating estimated glomerular filtration rate (eGFR). **Materials and Methods:** We prospectively analyzed 785 consecutive outpatients attending our department for cross-sectional examination. Multiple standard parameters were considered as risk factors for developing CIN. SC and eGFR values were obtained in patients sent for contrast examination. **Results:** A total of 234 (30%) patients were above 55 years of age; 122 (15.5%) had diabetes, of these 18 (15%) were on insulin. We found 167 (21.2%) patients with hypertension and 33 (4.2%) with known renal/cardiac diseases. Abnormal SC was found in 20 (3.9%) patients, and all these patients had at least one risk factor. No patient without any risk factor had abnormal SC. Based on eGFR, 204 (40%) patients had Stage 2, 46 (9%) patients had Stage 3, and 7 (1%) patients had Stage 4 renal dysfunction. Majority of patients (71%) with Stage 3 renal disease showed normal SC values. Only one patient under the age of 50 years without any risk factors had Stage 3 renal disease. **Conclusion:** Hypertension, diabetes, and advanced age are common risk factors for CIN in Indian population. Majority of patients with Stage 3 renal dysfunction have normal SC. Based on the study, we recommend measurement of SC/eGFR before giving intravenous contrast only in patients over the age of 50 years or those with known risk factors for CIN.

**Keywords:** Chronic kidney disease, computed tomography, contrast-induced nephrotoxicity, estimated glomerular filtration rate, serum creatinine

## INTRODUCTION

Contrast-induced nephropathy (CIN) is a sudden deterioration in renal function following the recent intravascular administration of iodinated contrast medium in the absence of another nephrotoxic event. CIN is one of the significant causes of morbidity in patients receiving intravenous contrast.<sup>[1,2]</sup> CIN is defined as absolute increase in serum creatinine (SC) values by  $\geq 0.5$  mg/dl or  $\geq 25\%$  from baseline values.<sup>[3,4]</sup> The incidence of CIN may be as low as 2% in patients without risk factors. But with risk factors, like diabetes, the number rises to 9% and 90% with diabetes with CKD.<sup>[5]</sup> The most common risk factors for CIN are preexistent renal insufficiency, diabetes mellitus (DM), hypertension, advanced age, nephrotoxic medications, dehydration, and heart diseases.<sup>[6-10]</sup> Advanced age has been variably defined as age  $>55$  years,<sup>[8]</sup>  $>60$  years,<sup>[2]</sup> and  $>70$  years.<sup>[9]</sup> In addition to the large number of risk factors, studies are further

complicated by the interrelationship between many of these risk factors.

In most institutes, SC levels are routinely obtained for all patients, before intravenous contrast-enhanced examinations as a method for assessing renal function and susceptibility for CIN.<sup>[1,2]</sup> SC on its own may not be a reliable measure of renal function as it has inherent limitations. Therefore, calculation of estimated glomerular filtration rate (eGFR) has important role in assessing the true renal function.<sup>[11-13]</sup> The American and Japanese society guidelines prefer eGFR threshold  $<60$  ml/min/1.73 m<sup>2</sup> for abnormal renal function.<sup>[3,4]</sup>

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**How to cite this article:** Auti OB, Manoj KV, Annapandian VM, Santosh Kumar DG, Murugan K, Karthik GA, *et al.* Routine screening of renal function before intravenous contrast examination: Is this required in the Indian scenario?. J Nat Sc Biol Med 2019;10:87-90.

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**Website:**  
www.jnsbm.org

**DOI:**  
10.4103/jnsbm.JNSBM\_27\_18

SC or eGFR measurements can be safely excluded in patients with the absence of risk factors according to some literature and guidelines from the American College of Radiology (ACR).<sup>[3]</sup>

In this study, we reviewed the renal profile of Indian patients attending our department. We aimed to determine whether SC levels are routinely required in all patients undergoing contrast examination and is there any added value of calculating eGFR in every patient. We also reviewed ACR and The Royal College of Radiologist (RCR) contrast administration guidelines and its applicability in the Indian population.

## MATERIALS AND METHODS

We prospectively analyzed 785 consecutive patients referred to the Department of Imaging for cross-sectional examination. Only outpatients were included in the study. Patients with non-Indian origin were excluded from the analysis. This study was considered as a departmental review, and patient consent was not deemed necessary. The study protocol was discussed and approved by the departmental ethics review board.

The data collected included age, history of diabetes, hypertension, renal/cardiac disease, dehydration, and/or nephrotoxic drug consumption. Insulin and oral hypoglycemic treatment history was obtained in patients with known diabetes. SC and eGFR levels were collected in all patients referred for contrast examination. Most recent laboratory values were considered and laboratory values more than 3 months old were excluded from the analysis.

Age >55 years was considered as a risk factor. Hypertension and diabetes risk factors were subjectively divided into the three groups well controlled, reasonably controlled, and poorly controlled according to patient's perception. Insulin and oral hypoglycemic treatment history was considered in patients with diabetes. Other risk factors were divided into the history of dehydration, presence of renal/cardiac diseases, and nephrotoxic drug consumption.

SC of  $\geq 1.5$  mg/dl was considered as abnormal.<sup>[4,13]</sup> Estimated GFR was classified according to Kidney Disease: Improving Global Outcome guidelines [Table 1].<sup>[14]</sup>

### Statistical analysis

Standard statistical methods for the assessment on proportions, percentages, and measures of central tendencies (mean and standard deviation) were used. Continuous variables were expressed as mean and interquartile range; categorical variables were expressed as frequency and percentage.

## RESULTS

Out of 785 patients, 484 (62%) were male with a male to female ratio of 1.6:1. The median age was 45 (range 2 months–98 years). A total of 234 (30%) patients were above 55 years of age and 29 were above 70 years. One hundred and twenty-two (15.5%) patients had DM, of these 18 (15%) were on insulin. Among these, 69 (56.5%) belonged

**Table 1: Stages of chronic kidney diseases according to the National Kidney Foundation-Kidney Disease Outcome Quality Initiative guidelines**

Stage	Description	GFR (ml/min/1.73 m <sup>2</sup> )
1	Kidney damage with normal or increased GFR	>90
2	Kidney damage with mild reduction in GFR	60-89
3	Moderate reduction in GFR	30-59
4	Severe reduction in GFR	15-29
5	ESRD or renal failure	<15 (or dialysis)

ESRD: End-stage renal disease, GFR: Glomerular filtration rate

to reasonably controlled group and 6 (5%) patients belonged to poorly controlled group. We found 167 (21.2%) patients with hypertension of which 88 (53%) belonged to reasonably controlled group. There were 33 patients (4.2%) with known renal/cardiac diseases, 35 (4.4%) with recent vomiting/diarrhea, and 10 (1.2%) with a positive history of long-term nephrotoxic drug consumption.

Out of 785 patients, 515 (65.6%) were referred for contrast examinations. Among these, 20 (3.9%) patients had abnormal SC. All of these 20 patients had at least one risk factor. Twelve (60%) patients had two or more risk factors and 8 (40%) had single risk factor. The known renal disease was the most common risk factor in this group of patients.

According to eGFR values, 258 (50%) patients had normal values. There were 204 (40%) patients with Stage 2, 46 (9%) with Stage 3, and 7 (1%) with Stage 4 renal dysfunction. There were no end-stage renal disease patients in the study group. All Stage 4 renal disease patients showed abnormal SC values. All patients in Stage 1 and Stage 2 renal disease had normal SC values. About 71% of patients with Stage 3 renal disease had normal SC values. Of these, only four patients were under the age of 55 years and did not have any risk factors for CIN.

## DISCUSSION

CIN is a serious condition associated with increased morbidity and mortality. In routine practice, all patients referred for intravenous contrast examination would undergo renal function test for the assessment of SC. To the best of our knowledge, this is the first study assessing risk factors for CIN in the Indian population to determine necessity of calculating SC in patients undergoing contrast studies.

CIN is commonly associated with patients who have risk factors such as age, DM, hypertension, and CKD. In our study population, advanced age of more than 55 years (30%) was the most common risk factor for CIN, followed by hypertension and DM. We found abnormal creatinine values in 4% of patients of which most common associated single risk factor was previous renal disease (62%). All patients with abnormal creatinine values had at least one risk factor and about 60%

**Table 2: The American College of Radiology and Royal College of Radiologist recommendations applied to our study group**

	Number of patients (who would not have had blood test)	With abnormal eGFR	Percentage risk
ACR			
Age <60 years without HT, DM, known renal disease	434	6 (all SC between 1 and 1.4)	1.4
RCR			
Age <70 years without DM, HT, known heart or renal disease	496	9 (all SC between 1 and 1.4)	1.8
Our recommendation			
Age <50 years without risk factors	353	1 (SC of 1.4)	0.28

ACR: The American College of Radiology, RCR: The Royal College of Radiologist, DM: Diabetes mellitus, HT: Hypertension, eGFR: Estimated glomerular filtration rate, SC: Serum creatinine

had multiple risk factors. We did not observe any abnormal creatinine values in patients under the age of 55 years.

Calculating eGFR can recognize patients with borderline renal function but normal SC. In our group, all patients with mild renal dysfunction (Stage 1 and 2) (eGFR 60–89 ml/min/1.73 m<sup>2</sup>) had normal creatinine values. This bodes well as CKD Stage 1 and 2 are not considered as an independent risk factor for CIN.<sup>[4]</sup> Stage 3 renal dysfunction (eGFR of < 60 ml/min/1.73 m<sup>2</sup>) are recognized risk factor for developing CIN. It is vital to recognize this group of patients before giving intravenous contrast so that appropriate precautions can be taken.<sup>[14-17]</sup> In our study, majority (71%) of patients with Stage 3 renal dysfunction had a normal creatinine. This incidence is alarmingly high compared to other published literatures with a reported incidence of 11.6%–13.6%.<sup>[13-18]</sup> These patients are often missed out if only SC levels are assessed to risk stratify for CIN. Some of these patients may not even have any other risk factors for CIN and will often go unrecognized. In our group, four patients in this group did not have any other recognized risk factor for CIN.

ACR and RCR have specific guidelines in assessing patients for CIN before giving contrast.<sup>[19,20]</sup> If these were to be applied to our population dataset, then six patients according to ACR guidelines and nine patients according to RCR guidelines with Stage 3 disease would have not been recognized to be at risk of CIN and would have undergone the examination with contrast [Table 2]. In our study, we found four patients under the age of 55 years without any risk factors with Stage 3 renal disease. In this group, three patients were between 50 and 55 years. If we consider the threshold of 50 years, only one patient would have gone unrecognized which gives the overall risk of 0.28%. This is much less compared to the risks we get after applying ACR or RCR guidelines in our study group which measured 1.4% and 1.8%, respectively.

Based on our observations, we would recommend that SC and eGFR should be calculated in all patients above the age of 50 years and in patients with known risk factor for CIN if under the age of 50 years.

The incidence of DM and unrecognized hypertension is relatively high in Indian patients. Therefore, the findings of

this study are not a major surprise. Authors do recognize the limitations of this study, which includes modest number of cases and lack of longitudinal follow-up of the patients to assess the development of CIN. Appropriate management of patients at risk of CIN is beyond the scope of this study. Inpatients were not included in the study, as they often have questionable hydration status and may be receiving multiple medications which may interact with renal function.

## CONCLUSION

The incidence of occult renal dysfunction is high in the Indian population. Hypertension, DM, and advanced age are the most common risk factors for CIN in the Indian population. eGFR should be calculated in all patients having SC assessment. Both SC and eGFR should be calculated in all patients above the age of 50 years and in patients with known risk factor for CIN if they are below 50 years of age.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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