

# Assessment of the Radio-contrast Media-Induced Self-Reported Adverse Drug Reactions in a Tertiary Care Hospital of North India: A Prospective Study

## Abstract

**Background:** Radio-contrast media are the agents which are used on daily basis in the radiological practice for either diagnostic or therapeutic purpose. Currently used agents are considered to be safe but not devoid of side effects. **Objectives:** Objectives of the study were to assess the incidence of adverse drug reactions (ADRs) in the patients who receive radiographic contrast media for computed tomography (CT) and intravenous pyelography (IVP), to stratify the ADRs into different types based on their time of appearance and as per their severity. **Materials and Methods:** A prospective and observational study of 1-year duration was done on all the patients who received radio-contrast media (Iohexol) intravenously for CT and IVP in the radiodiagnosis department. Patients who experienced ADRs were recorded for the basic demographic characteristics and types of ADRs. Stratification of ADRs as per their severity was done using common terminology criteria for adverse events scale and Modified Hartwig and Siegel ADR Severity Assessment Scale, and casualty assessment was done using Naranjo's Algorithm. **Results:** Out of the total 3522 patients who were included in the study, eight patients got 12 suspected ADRs with some of the patients having more than one type of ADR. The most frequent ADR was nausea and vomiting (25%), followed by fever, chills, or sweating. Incidence of ADRs was 0.23%. All the ADRs were acute and occurred within 30 min of contrast administration. As per the severity scales used, all the ADRs were mild (75%) to moderate (25%) in nature with none of the reactions to be severe. Causality assessment showed 87.5% of the reactions to be "probable" in nature. **Conclusion:** Low osmolar nonionic radio contrast media are associated with very low incidence of ADRs in the North Indian population.

**Keywords:** Adverse drug reactions, causality, iohexol, low osmolar contrast, radio-diagnosis

## Introduction

With the advancement in the clinical imaging applications, there is a tremendous increase in the use of radio-contrast agents.<sup>[1]</sup> Radio-contrast agents are the drugs that allow the visualization of different structures such as internal organs of the body.<sup>[2]</sup> They are the one that contrast the selected areas of body from the surrounding tissue, thus enhancing the visibility of specific organs, blood vessels, or tissues.<sup>[3]</sup> For intravenous administration, currently used contrasts are the iodinated agents. They are the derivatives of tri-iodobenzoic acid.<sup>[4]</sup> These iodinated contrast agents are divided into ionic and nonionic (on the basis of charge of the iodinated molecule), monomeric and dimeric (on the basis of molecular structure), and hyperosmolar, low osmolar, and iso-osmolar (on the

basis of osmolality).<sup>[5]</sup> Nowadays, nonionic and low or iso-osmolar contrast agents are used intravenously in radio-diagnosis for imaging modalities such as computed tomography (CT) scan and intravenous pyelography (IVP).<sup>[1]</sup> These agents are considered to be safer than the hyperosmolar agents. However, iso-osmolar or low osmolar contrast agents are not devoid of side effects though account for low incidence of ADRs. The adverse drug reactions (ADRs) to these agents can vary from mild reactions requiring no intervention to the rare life-threatening situations.<sup>[6]</sup>

Cognizance of different types of ADRs that can occur with the use of contrast agents is the utmost requirement for the radiologist so that the timely intervention is prompted. Little attention is given to identify and notify ADRs associated with radio-contrast

**Pushpinder Singh,  
Manraj Kaur Gill,  
Mandeep Kaur<sup>1</sup>,  
Rajiv Mahajan<sup>1</sup>,  
Manjot Kaur**

*Departments of Radiodiagnosis and <sup>1</sup>Pharmacology, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India*

**Submitted:** 09-Jun-2021  
**Revised:** 15-Sep-2021  
**Accepted:** 09-Nov-2021  
**Published:** 31-Jan-2022

**Address for correspondence:**  
Dr. Manraj Kaur Gill,  
Adesh Institute of Medical  
Sciences and Research,  
Bathinda, Punjab, India.  
E-mail: manrajkaurgill2021@  
gmail.com

### Access this article online

**Website:**  
[www.ijabmr.org](http://www.ijabmr.org)

**DOI:**  
10.4103/ijabmr.ijabmr\_381\_21

### Quick Response Code:



**How to cite this article:** Singh P, Gill MK, Kaur M, Mahajan R, Kaur M. Assessment of the radio-contrast media-induced self-reported adverse drug reactions in a tertiary care hospital of North India: A prospective study. *Int J App Basic Med Res* 2022;12:14-7.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

media in particular, as they are used in diagnostic medicine and not in clinical care medicine in proper. This may be due to lack of follow-up in the radiology department. Hence, this study was done to assess the incidence of ADRs in a tertiary care hospital in North India and to know the causality and severity of the reactions caused by the nonionic and low osmolar contrast agent.

## Materials and Methods

### Study design

An observational and prospective study was done for a period of 1 year in the department of radio diagnosis in a tertiary care hospital of North India. The study was initiated after obtaining the approval of Institutional Ethics committee.

### Patient selection

#### Inclusion criteria

All the patients who were referred to the department of radio-diagnosis by the clinician for contrast-enhanced CT (CECT)/IVP were observed and those patients who developed ADRs were included in the study after getting informed oral consent.

#### Exclusion criteria

Patients with a known case of renal disease and history of allergy to drugs/contrasts in the past were excluded from the study.

### Contrast media used

Iohexol 300 was used as radio-contrast media which contains 300 mg/ml dose. Patients were given IV dose as per their body weight. Usual dose of iohexol was kept in the range of 1–2 ml/Kg body weight. Total dose given to the patients varied within this range depending on the type of investigation and body habitus.

### Study assessments

All the ADRs which were spontaneously reported were recorded and analyzed. The investigators assisted the patient in filling the medicines side effect reporting form (for consumers) developed by Indian Pharmacopoeia, National Co-coordinating Centre-Pharmacovigilance Programme of India, Ministry of Health and family Welfare, and Government of India which can be downloaded from the official website of IPC [www.ipc.gov.in](http://www.ipc.gov.in). The patients were counseled as well as observed for any ADR they may encounter after the administration of the contrast media.

Severity of the ADRs was evaluated through two scales; common terminology criteria for adverse event (CTCAE) and Modified Hartwig and Siegel Severity Assessment Scale, and casualty assessment was done using Naranjo's.<sup>[7-9]</sup> Algorithm.

### Statistical analysis

Data were analyzed using Microsoft Excel 2010 (Microsoft Office, Version 14.0.4, 2010 Microsoft Corporation, Redmond, Washington, United States) and were represented as frequencies and percentages. Chi-square test was used for statistical evaluation.  $P < 0.05$  was considered statistically significant.

### Results

A total of 3522 patients received radio-contrast agents to carry out CECT/IVP for diagnostic purposes in a period of 1 year. The incidence of ADRs that occurred in this time period was 0.23% (8/3522). Basic demographic characteristics of our study population and patients with ADRs are summarized in Table 1. Out of total study population ( $n = 3522$ ), 2076 (58.94%) were male patients and 1446 (41.1%) were females. Among 2076 male patients, 05 (0.24%) patients developed ADR, and out of the 1446 female patients, 03 (0.21%) patients developed ADRs.  $P$  value was calculated ( $P = 0.877$ ), and it was inferred that the gender of the patient was not significantly associated with the development of ADRs [Table 1].

Patients in third and fourth decades of life had experienced more number of ADRs in our study as compared to other.  $P$  value was calculated ( $P = 0.868$ ) and it was inferred that the age group of the patient was also not significantly associated with the development of ADRs.

Majority of the ADRs ( $n = 7$ ) were immediate that occurred within 5 min of contrast administration. One ADR was intermediate that developed in 15–20 min of contrast administration. None of the patient developed delayed ADRs<sup>[10]</sup>.

**Table 1: Demographic characteristics of study population**

Characteristics	Number of patients with ADR ( $n=8$ ), $n$ (%)	Number of patients without ADR ( $n=3514$ ), $n$ (%)	Total ( $n=3522$ ), $n$ (%)
Gender			
Male	5 (0.24)	2071 (99.76)	2076 (58.94)
Female	3 (0.21)	1443 (99.79)	1446 (41.06)
$P=0.877$			
Age (years)			
21-30	1 (0.16)	610 (99.84)	611 (17.35)
31-40	3 (0.38)	794 (99.62)	797 (22.63)
41-50	2 (0.25)	790 (99.75)	792 (22.49)
51-60	1 (0.14)	709 (99.86)	710 (20.16)
>60	1 (0.16)	611 (99.84)	612 (17.38)
$P=0.868$			

ADR: Adverse drug reactions

### Severity assessment

According to CTCAE scale, six patients had mild reactions and two patients had moderate reactions. Similar results were obtained from modified Hartwig and Siegel Severity Assessment Scale. Majority of the ADRs (75%) were classified at level-1 score which denoted the reactions to be mild in nature and 25% were labeled at level-3 [Table 2]. On interpretation of results of patients with level-3 score, these patients were sorted into the category of moderate reactions. In the eight patients who reported ADRs, total 12 suspected reactions were seen. Mild reactions included the fever, chills, nausea/vomiting, rash, epigastric pain, and headache. These reactions were self-limiting requiring no medical intervention. Moderate reactions included hoarseness of voice experienced by one patient and sweating along with intense shivering experienced by other patient [Table 3]. Both these reactions needed immediate medical treatment in the form of corticosteroids and antihistaminics.

### Causality assessment

Naranjo's Algorithm scale was used to see the extent of relationship between a drug and a suspected reaction. It is the simple, less time consuming, and most commonly used scale in clinical practice.<sup>[11,12]</sup> It revealed that majority of the reactions were "probable" in nature [Figure 1].

### Discussion

Majority (62.5%) of the patients with ADRs were in the age group of 31–50 years. The present observation correlates well with the study done by Chopra *et al.* on North Indian population.<sup>[12]</sup> Another study by Modi *et al.*<sup>[13]</sup> also depicted that the ADRs are more common in the third and fourth decades of life. In our study, only two patients had the ADRs above 50 years of age, and it is comparable with the study done by Patel *et al.* who showed similar results.<sup>[6]</sup> According to our study, ADRs were more frequent in males ( $n = 5$ ) than females ( $n = 3$ ). This is in accordance with the study by Bhowmick *et al.*<sup>[14]</sup> conducted for 1 year.

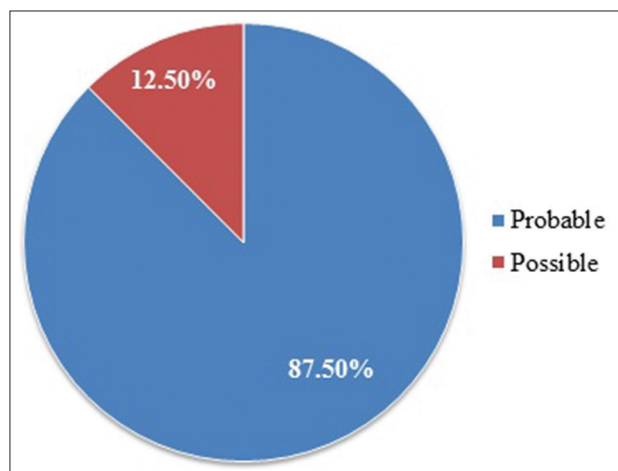


Figure 1: Causality assessment using Naranjo's Algorithm

The incidence of ADRs was low (0.23%) in our study with the use of Iohexol as radio-contrast agent. The low incidence correlates with the incidence of 0.3% shown by Bhowmick *et al.*<sup>[14]</sup> who conducted the study for a period of 1 year with two types of nonionic low osmolar radio-contrast agents. Low incidence might be attributed to the property of low osmolarity and increased solubility of these agents contributing to less toxicity.<sup>[15]</sup> According to the study by Gharekhanloo *et al.*<sup>[16]</sup> on comparison between iso-osmolar and low osmolar radio-contrast agent, iso-osmolar agents are considered to be much better tolerated than low osmolar agents. To have a confirmatory evidence of the above fact, the authors of this study are engaged in other observational study comparing the adverse effects between the iso and low osmolar radio-contrast agents.

In our study, all the ADRs appeared within a time period of 1 h which is in accordance with the study by Patel *et al.*<sup>[6]</sup> where all the general reactions were acute in nature. Out of 12 suspected ADRs, majority were nausea and vomiting followed by fever/chills or sweating further supported by the study done by Inbaraj *et al.*<sup>[17]</sup> where majority of the patients presented with nausea and vomiting as the main ADR following administration of intravenous contrast agent.

Table 2: Severity assessment of radio-contrast media induced adverse drug reactions

Severity scales	Number of cases with ADRs ( $n=8$ ), $n$ (%)
CTCAE scale	
Mild	6 (75)
Moderate	2 (25)
Severe	0
Modified Hartwig and Siegel ADR Severity Assessment Scale	
Level 1	6 (75)
Level 2	0
Level 3	2 (25)
Level 4	0
Level 5, 6 and 7	0

ADR: Adverse drug reactions, CTCAE: Common terminology criteria for adverse events

Table 3: Number of adverse drug reactions developed in patients

ADRs	Number of patients, $n$ (%)
Nausea/vomiting	3 (25)
Fever/chills	2 (16.67)
Sweating	2 (16.67)
Shivering	1 (8.33)
Epigastric pain	1 (8.33)
Headache	1 (8.33)
Rash	1 (8.33)
Hoarseness of voice	1 (8.33)

ADRs: Adverse drug reactions

As per the severity assessment scales used in our study, majority of the ADRs (75%) were mild in nature followed by 25% moderate reactions and no severe reactions. Similar observations were noted in Inbaraj *et al.*<sup>[17]</sup> study with the use of intravenous contrast where most of the ADRs were in the mild-to-moderate category. It is quite evident from the above observations that the nonionic and low osmolar contrast agents are much safer and devoid of severe reactions. It is further supported by the study done by Patel *et al.*,<sup>[6]</sup> where majority of the reactions were moderate in nature and none were severe.

Causality assessment of the ADRs was done for each ADR report using Naranjo's Algorithm scale. Out of 8 cases, 7 had a score of 5 which means they all are "probable" in nature. This signifies that though not proven, drug is likely the cause of the event. One case had a score of 4 which denoted that it is "possible" in nature. It means drug as well as well as other causes could be responsible for the event. This is in contrary to the study done by Bhowmick *et al.*<sup>[14]</sup> where all 11 ADRs were reported to be possible in nature. However, the observations of our study are in accordance with the research done by Patel *et al.*<sup>[6]</sup> where 100% of the ADRs were "probable" in causality as per the Naranjo's Algorithm.

### Conclusion

This observational study indicates that the use of nonionic low osmolar radio-contrast media is associated with very low incidence of ADRs which varies from mild-to-moderate reactions. But still, the radiologists and radiographers involved in the administration of radio-contrast agents must be aware of all types of ADRs so that timely intervention can be executed.

### Ethical clearance

Study was conducted after approval from Ethics Committee of Adesh University, Bathinda.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Beckett KR, Moriarity AK, Langer JM. Safe use of contrast media: What the radiologist needs to know. *Radiographics* 2015;35:1738-50.

2. Michele A, Teresa F, Giovanbattista D, Ashour M. The toxicity of iodinated radiographic contrast agents in the clinical practice. *J Nephrol Adv* 2017;1:6-41.
3. Andreucci M, Solomon R, Tasanarong A. Side effects of radiographic contrast media: Pathogenesis, risk factors, and prevention. *Biomed Res Int* 2014;2014:741018.
4. Dickinson MC, Kam PC. Intravascular iodinated contrast media and the anaesthetist. *Anaesthesia* 2008;63:626-34.
5. Thomsen HS, Morcos SK. Radiographic contrast media. *Br J Urol* 2000;86 Suppl 1:1-10.
6. Patel M, Pillai A, Kausar F. A study of adverse drug reactions to iodinated contrast agents in tertiary care teaching hospital. *Int J Basic Clin Pharmacol* 2019;8:2440-4.
7. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0. NIH Publication 09-7473. Rockville: Institutes of Health, US Department of Health and Human Services; 2017. Available from: [https://ctep.cancer.gov/protocolDevelopment/electronic\\_applications/docs/CTCAE\\_v5\\_Quick\\_Reference\\_5x7.pdf](https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf). [Last accessed on 2020 Oct 05].
8. Petrova G, Stoimenova A, Dimitrova M, Kamusheva M, Petrova D, Georgiev O. Assessment of the expectancy, seriousness and severity of adverse drug reactions reported for chronic obstructive pulmonary disease therapy. *SAGE Open Med* 2017;5. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5308439/>. [last accessed on 2022 Jan 16].
9. Srinivasan R, Ramya G. Adverse drug reaction-causality assessment. *Int J Res Pharm Chem* 2011;1:606-12.
10. ACR Manual on Contrast Media. *Acr.org*; 2021. Available from: [https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast\\_Media.pdf](https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf). [Last accessed on 2021 Sep 15].
11. Kyung EJ, Ryu JH, Kim EY. Evaluation of adverse reactions to contrast media in the hospital. *Br J Radiol* 2013;86. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3856550/>. [last accessed on 2022 Jan 16].
12. Nirumalla M, Sanapala S, Bobbili SV, Unni VK, Prathyusha P. A prospective study of adverse drug reactions in a tertiary care hospital in patients. *Pharm Innov* 2019;8:277-86.
13. Modi NB, Vaidya K, Dudhia S, Shah RB, Date SK. A study of adverse drug reactions to radiocontrast media in a tertiary care teaching rural hospital. *Int J Med Sci Public Health* 2014;3:133-6.
14. Bhowmick S, Bhat E, Panja B, Mukherjee S, Sikdar S, Biswas A, *et al.* A study on adverse drug reactions to non-ionic contrast medium in an Indian population: A 1-year experience. *Int J Basic Clin Pharmacol* 2014;3:1066-71.
15. Roh S, Laroia A. Practicing safe use of nonionic, low-osmolality iodinated contrast. *Appl Radiol* 2015;44:16-9.
16. Gharekhanloo F, Torabian S. Comparison of allergic adverse effects and contrast enhancement between iodixanol and iopromide. *Iran J Radiol* 2012;9:63-6.
17. Inbaraj SD, Sidhu Ganesh R, Muthiah NS. Pharmacovigilance of radiographic contrast-induced adverse drug reactions in a tertiary care hospital of South India. *Asian J Pharm Clin Res* 2017;10:364.