International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

A Retro-Prospective Observational Study to Evaluate the Radiocontrast Media-Induced Adverse Drug Reactions in a Tertiary Care Hospital

Afrah Ashraf, Syed Junaid Bilal, Sumayya Younus, Mahamadi Shaguftha, Dr. A.V.Kishore Babu, Dr. Mohammed ZiaUddin

[1,2,3,4]*Student, Bhaskar Pharmacy College, Telangana*
[5]*HOD, Department of Pharmacy Practice, Bhaskar Pharmacy College, Telangana.*
[6]*HOD, Senior Clinical Pharmacologist, Apollo Hospitals, Hyderabad.*
Corresponding Author: Afrah Ashraf

Date of Submission: 10-06-2024 Date of Acceptance: 20-06-2024

ABSTRACT: **BACKGROUND:** The development of clinical imaging applications has led to a significant increase in the use of radiocontrast agents. Although iodinated radiocontrast media (IRCM) are generally considered safe, adverse drug reactions may still occur with their wide use in current clinical practice.

OBJECTIVES: The objectives of the study were to assess the patients experiencing ADRs after undergoing contrast-enhanced computed tomography (CECT), to determine the causality and severity of the adverse drug reactions with the use of radiocontrast media, as well as to identify risk factors for the occurrence of Hypersensitivity reactions and preventive measures for it.

METHODOLOGY: The study was commenced after obtaining permission and approval from the Institutional Ethics Committee on Biomedical Research (IEC-BMR) of Apollo Hospitals Hyderabad. The data of patients with ADR following radiocontrast administration was collected from the patient's medical records. The study was conducted retrospectively and prospectively. Retrospective data was collected from the reported ADRs from the clinical pharmacology department. Prospectively, all the eligible patients who were willing to participate were included in the study after obtaining an informed consent form. The data has been collected from the CT scan room of the reported ADR following the radiocontrast administration. All the enrolled patients included in the prospective study were provided with counselling on precautions and common dos and don'ts after the radiocontrast administration.

RESULTS: Out of total 300 patients who were assessed, 113 patients experienced ADRs with some of the patients experiencing more than one type of ADR. The most frequent ADR was a sensation of warmth throughout the body (49.5%), followed by headache (19%) and chills (11.5%). Other ADRs included dizziness, anxiety, and nausea which were less frequent. Only one patient experienced extravasation and one patient had an anaphylactic reaction, which was immediately treated.

All the ADRs were immediate in type and occurred within the first hour of contrast administration. As per the severity scale used in the study, the majority of the ADRs were classified as 'Grade-1' or 'mild' (96%) to moderate (3.5%) with no severe reactions. Causality assessment done using Naranjo's algorithm scale showed 100% of the cases as "possible" and the WHO-UMC scale showed all cases to be "probable" in nature.

CONCLUSION: In conclusion, the frequency of all types of adverse reactions is significantly decreased by the use of non-ionic, low osmolar radiocontrast agents. The majority of these reactions were of immediate type. The pharmacological prevention provided to high-risk patients is another factor in preventing adverse reactions.

KEYWORDS: Adverse drug reactions, hypersensitivity reactions, iodinated radiocontrast media, low-osmolar contrast media, contrast-enhanced computed tomography.

I. INTRODUCTION

In modern clinical practice, iodinated radiocontrast media are frequently employed. Despite being usually safe, iodinated radiocontrast

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

media may still cause major adverse drug reactions. Drugs known as radio-contrast agents make it possible to see various human organs and other structures. More than 75 million times a year, radiocontrast media are used to improve radiography pictures, and it is well-recognized that radiocontrast media administration frequently results in unpleasant effects.[1,4] A serious health concern is the rise in the frequency of hypersensitivity reactions to iodinated contrast medium over the past few years. Depending on whether they occur within an hour or more of Iodinated contrast media administration, Hypersensitivity reactions to iodinated contrast media are classified as either immediate or non-immediate, as well as monomeric, and dimeric (based on molecular structure), hyperosmolar, low osmolar, and iso-osmolar (based on osmolality).[1,2]

Examining ICM safety profiles is crucial for the prevention and best management of Iodinated contrast media-related Hypersensitivity reactions due to the high volume of contrast agent-enhanced CT scans that are conducted.[3] Skin is the organ that experiences reactions the most frequently, ranging in severity from moderate to severe. [2] It is considered that delayed reactions are likely just as frequent as acute adverse reactions, if not more so. Mild maculopapular exanthema is the most common clinical manifestation of delayed hypersensitivity reactions.[4] The use of the offending Iodinated contrast media must be prohibited in order to manage patients who have been identified as having Hypersensitivity reactions to Iodinated contrast media, and non-cross-reactive medications must be found that the patient can use without risk. There are debates going on right now over the cross-reactivity pattern. Iodixanol, iopamidol, iomeprol, iohexol, ioversol, and ioxitalamate frequently cross-react with one another. The most frequent relationship between iodixanol and iohexol, the monomer of iodixanol, has been reported, suggesting that cross-reactivity is related to the chemical structure of Iodinated contrast media.[2]

These days, non-ionic and low or iso-osmolar contrast chemicals are administered intravenously for radiodiagnosis when using imaging modalities including intravenous pyelography and computed tomography scans. These substances are thought to be less dangerous than hyperosmolar substances. Although they contribute to the low frequency of ADRs, iso-osmolar or low osmolar contrast agents are not without risk of side effects. These drugs can cause adverse drug reactions that range from minor side effects that don't need treatment to extremely uncommon life-threatening events.[1]

This study is being carried out in a tertiary care hospital to ascertain the causality and severity of the responses caused by the different types of radiocontrast agents, as well as to identify risk factors for the occurrence of Hypersensitivity reactions and preventive measures for the same.

II. METHODOLOGY

SAMPLE SIZE:

The number of patients included in this study was 300.

STUDY CRITERIA:

INCLUSION CRITERIA:

1. All patients who will be sent to the radiology department for contrast-enhanced CT (CECT) by the clinician will be monitored, and those who experience adverse drug reactions will be added to the study after obtaining their consent.
2. Patients willing to participate in the study.

EXCLUSION CRITERIA:

1. Patients undergoing CT scans without contrast.
2. Pregnant women.
3. Patients with a history of allergy to contrasts in the past.
4. Patients with a recent history of contrast extravasation.
5. Patients who are not conscious.

SOURCE OF DATA COLLECTION:

STUDY MATERIAL: Data of patients who had ADR after receiving radiocontrast will be collected from the patient's medical record. Both retrospective and prospective approaches will be used in the study. From the clinical pharmacology department's reported ADRs, retrospective data will be gathered. After receiving an informed consent form, the study will prospectively enroll all eligible patients who are willing to take part. Following the administration of radiocontrast, the data will be collected from the CT scan room of the reported ADR. After the radiocontrast administration, all enrolled patients included in the prospective study will get counselling on precautions and typical dos and don'ts.

STATISTICAL ANALYSIS:

The obtained data will be entered into MS EXCEL 365. Quantitative variables will be summarized

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

using descriptive statistics. The data will be statistically analysed and will be represented as graphs, pie diagrams, and bar graphs.

OUTCOME MEASURES:

1. Percentage of radiocontrast induced adverse drug reactions
2. Percentage of adverse drug reactions occurrence.
3. Percentage of occurrence of various categories of causality in reported ADRs
4. The presence or absence of immediate reactions during or immediately after the procedure.

III. RESULTS

In our current observational study, a total of 300 patients visiting the radiology department for contrast-enhanced CT (CECT) were assessed, out of which 113 patients experienced ADRs. The causality and severity of the adverse drug reactions experienced by these patients were evaluated and categorised accordingly.

Radio contrast media-induced adverse drug reactions:

No. of patients who received CECT	No. of patients who experienced ADR	Percentage (%)
300	113	37.6%

Table-4 Total no. of participants and no. of participants who experienced ADR

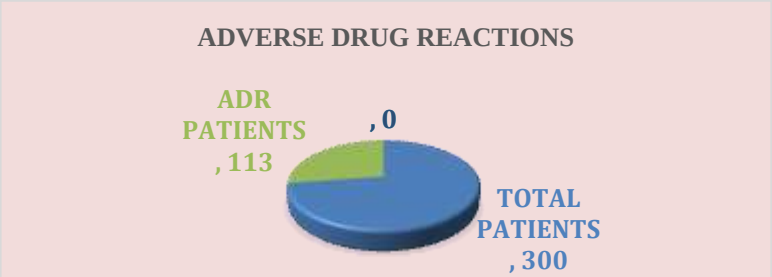

Fig-7: The total number of patients who underwent CECT in our study was 300, out of which 113 patients had experienced ADR after the administration of radiocontrast media. The percentage of radiocontrast-induced adverse drug reactions is 37.6%

- **GENDER-WISE DISTRIBUTION OF PATIENTS:**

Table-5: Distribution of subjects based on sex.

GENDER	NO. OF PATIENTS	PERCENTAGE (%)
MALE	77	68
FEMALE	36	32
TOTAL	113	100

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

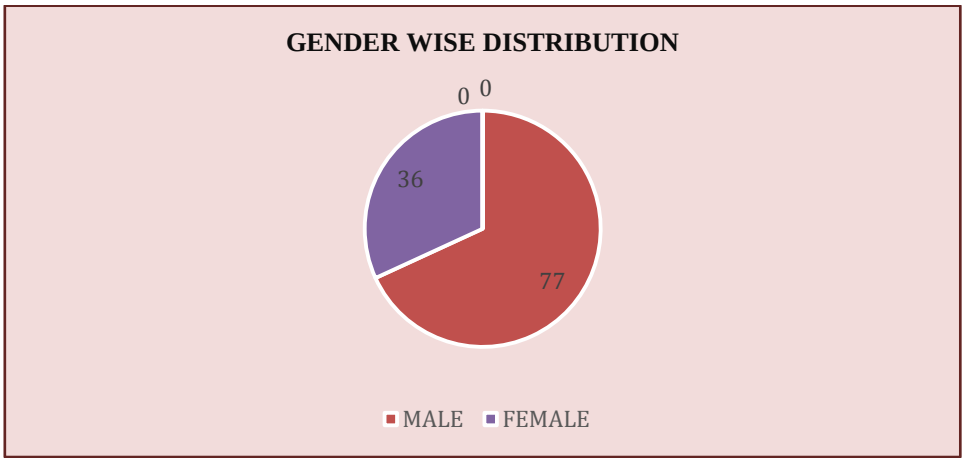

Figure-8: Gender-wise distribution of patients.

➢ **AGE-WISE DISTRIBUTION OF PATIENTS:**

Thepatients were divided into 4 groups based on their age

AGE (YEARS)	MALE	FEMALE	TOTAL	PERCENTAGE (%)
<19	3	0	3	2.6%
19-39	21	10	31	27.4%
40-59	35	16	51	45%
>60	19	9	28	25%

Table-6: Distribution of subjects based on age group

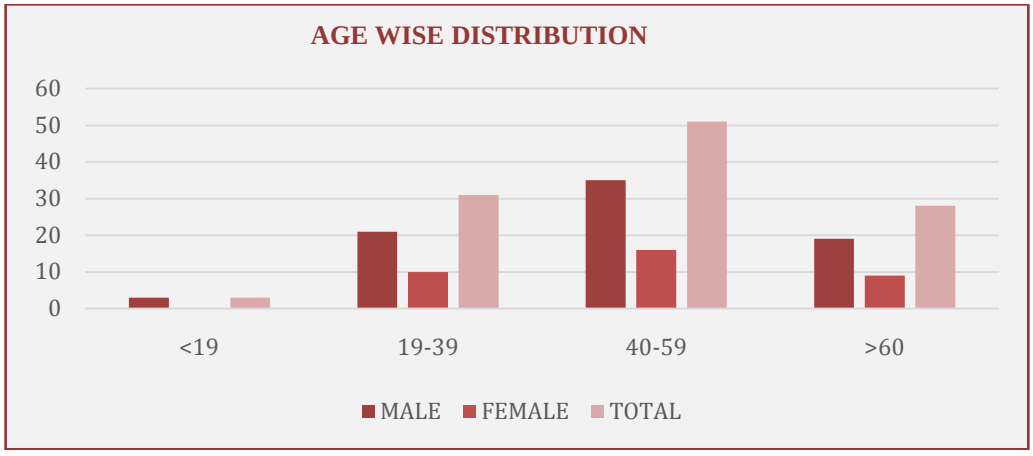

Figure-9: Age wise distribution of patients

Out of all patients, most of the patients who experienced ADR were in the age group of 40-59 years (45%) followed by 19-39 years (27.4%).

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

➢ **COMORBID CONDITIONS-WISE DISTRIBUTION OF PATIENTS:**

Comorbidities	Male	Female	Total	Percentage (%)
Hypertension	11	7	18	15.9%
Diabetes	12	6	18	15.9%
Asthma	4	2	6	5.3%
Hypothyroidism	0	3	3	2.6%

Table-7: Distribution of patients based on their comorbidities

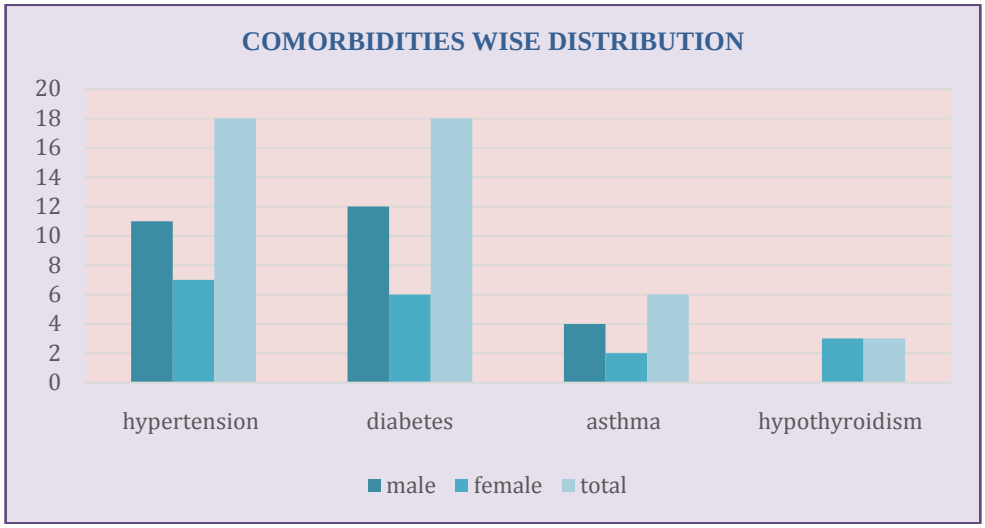

Figure-10: Comorbidities-wise distribution of patients

Out of all patients, most of the patients were found to be with diabetes (15.9%) and hypertension (15.9%)

➢ **DISTRIBUTION BASED ON THE ROUTE OF ADMINISTRATION:**

Table-8 distribution based on ROA

ROA	NO OF PATIENTS	PERCENTAGE (%)
IV	95	84%
ORAL & IV	18	16%
RECTAL	0	0%

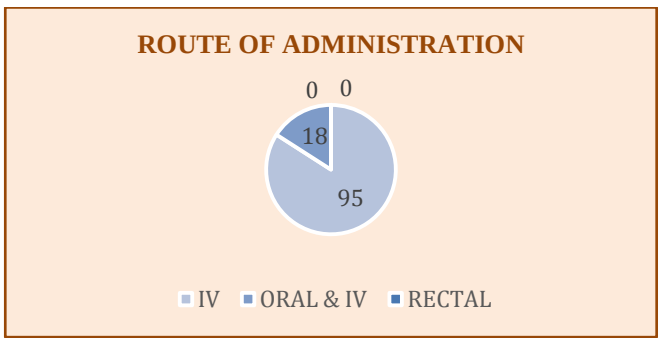

Figure-11: The patients were divided according to ROA, most of the patients administered the drug were through the IV route (84%)

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

➢ **TYPES OF CONTRAST MEDIA USED:**

Type of contrast media	No of the patients administered	Percentage (%)
Iohexol	112	99%
Iodixanol	1	1%

Table-9 distribution based on type of contrast used

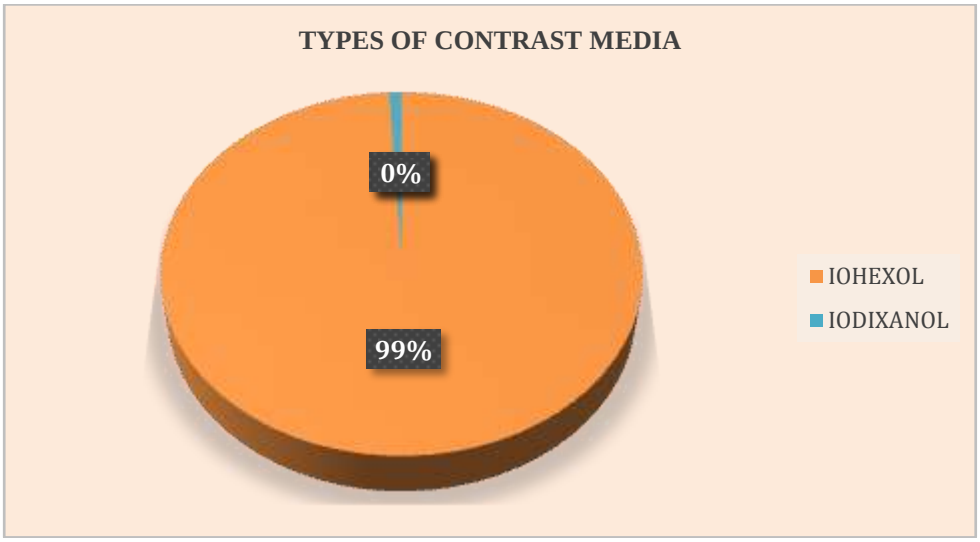

Fig-12The patients were divided based on the type of contrast administered to them, and 99% of them were given iohexol.

➢ **ADR OCCURRENCE:**

ADR	No of patients	Percentage (%)
Warmth	56	49.5%
Headache	22	19%
Chills	13	11.5%
Dizziness	10	9%
Anxiety	5	4.4%
Shivering	3	2.6%
Nausea	1	0.8%
Extravasation	1	0.8%
Anaphylactic reaction	1	0.8%
Flushing	1	0.8%

Table-10 distribution based on ADR

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

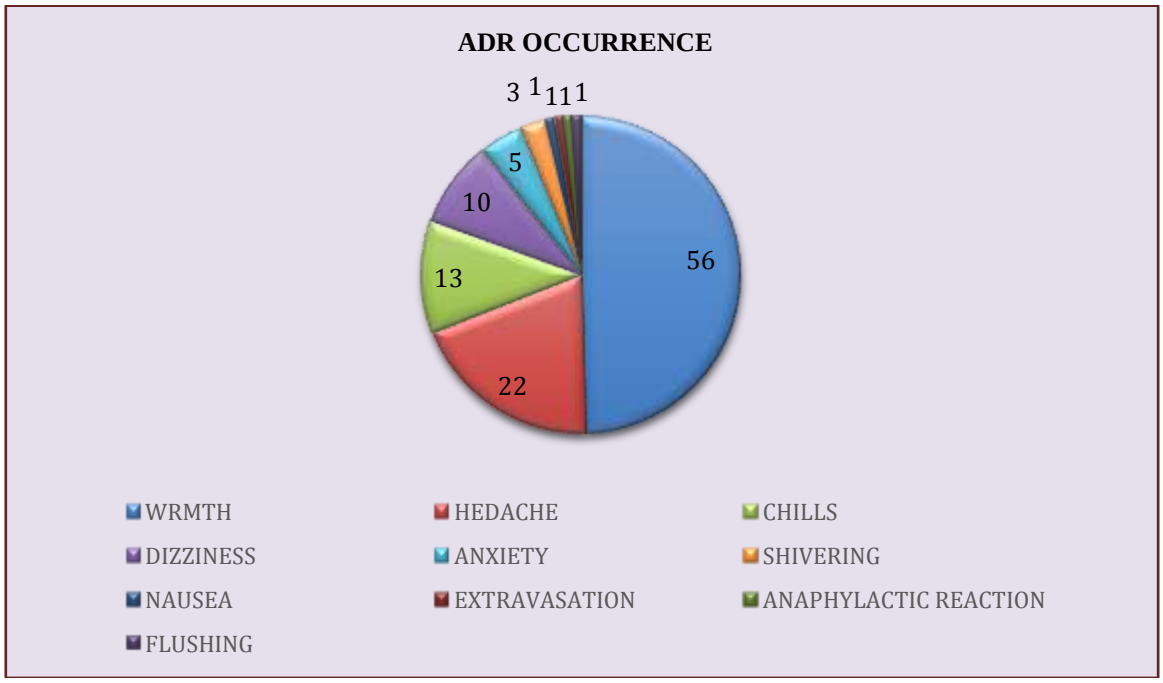

Figure-13: Out of all possible ADRs, the most commonly occurred ADR was warmth (49.5%)

➢ **DISTRIBUTION BASED ON THE TYPE OF REACTION:**

Type of reaction	No of patients	Percentage (%)
Immediate	113	100%
Delayed	0	0%

Table-11: distribution based on type of reaction

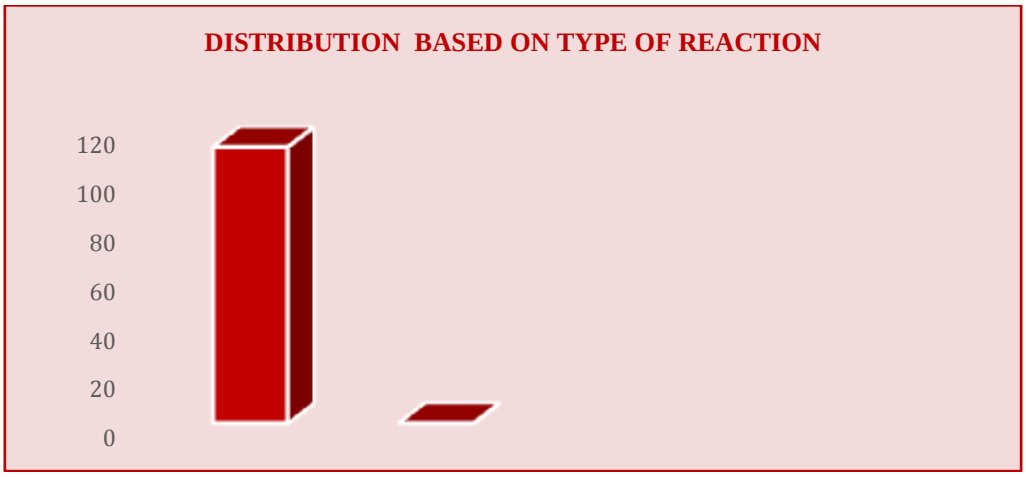

Figure-14: The patients were divided according to the type of reaction, 100% of the patients experienced an immediate reaction

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

➢ **DISTRIBUTION BASED ON THE SEVERITY OF AN ADR (CTCAE):**

CTCAE	No. of patients	Percentage %
Grade 1	109	96%
Grade 2	0	0%
Grade 3	4	3.5%
Grade 4	0	0%
Grade 5	0	0%

Table-12 distribution based on the severity of ADR

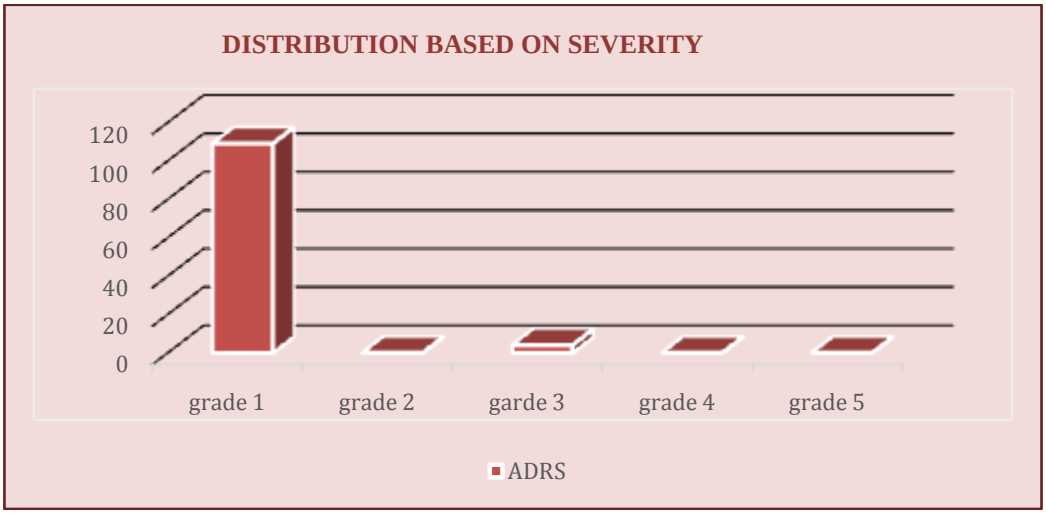

Figure-15: The patients were divided according to the severity of the ADR, most of the patients were mildly affected (96%)

➢ **CAUSALITY ASSESSMENT (NARANJO SCALE):**

NARANJO SCALE	NO. OF ADRs	PERCENTAGE (%)
DEFINITE	0	0%
PROBABLE	0	0%
POSSIBLE	113	100%
DOUBTFUL	0	0%

Table-13 causality assessment using Naranjo scale

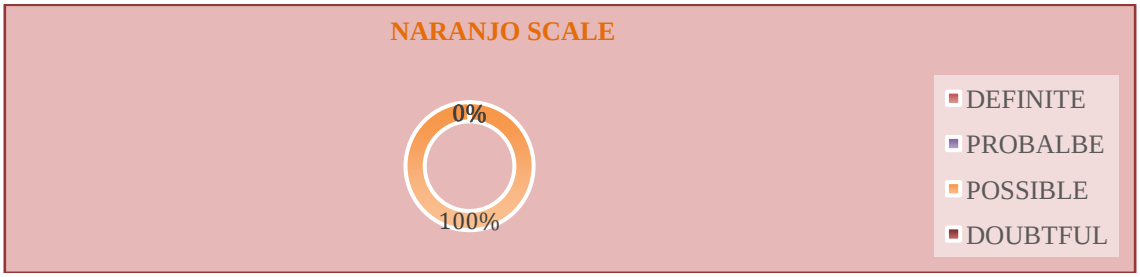

Figure-16 Causality assessment using Naranjo's Algorithm Scale

Out of 113 patients, 100% had a score of 4 which means they are all "possible" in nature.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

- **CAUSALITY ASSESSMENT (WHO SCALE):**

WHO SCALE	NO OF ADRs	PERCENTAGE (%)
Certain	0	0%
Probable/Likely	113	100%
Possible	0	0%
Unlikely	0	0%

Table-14 causality assessment using WHO scale

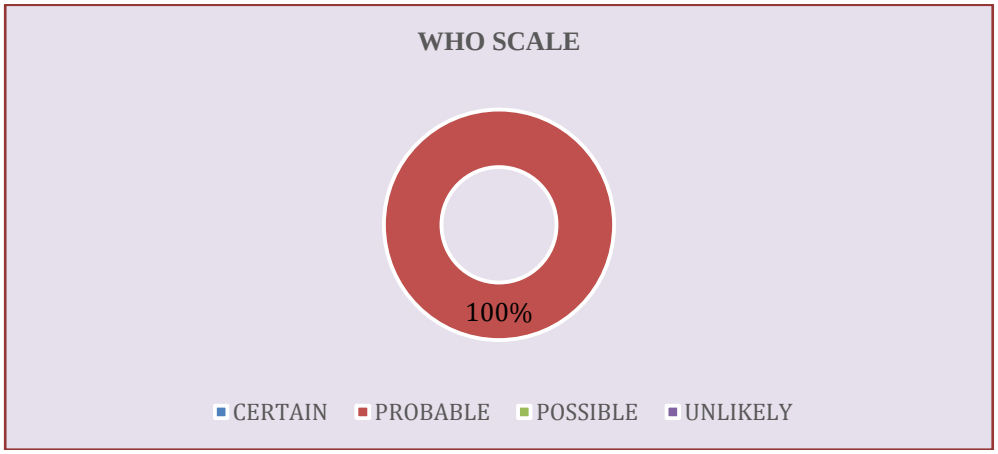

Figure-17 Severity assessment based on the WHO algorithm

Out of 113 patients, 100% were “probable” in nature.

- **DISTRIBUTION BASED ON PHARMACOLOGICAL PREVENTION:**

Patients who are at risk of adverse reactions to contrast are recommended to take premedication.

Drug (premedication)	Indication	No of patients	Percentage (%)
BETALOC INJ	To treat arrhythmia	9	8%
SORBITRATE TAB	To prevent angina attacks	22	19%
HYDROCORTISONE INJ	To treat asthma	6	5%

Table-15 distribution based on pharmacological prevention

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

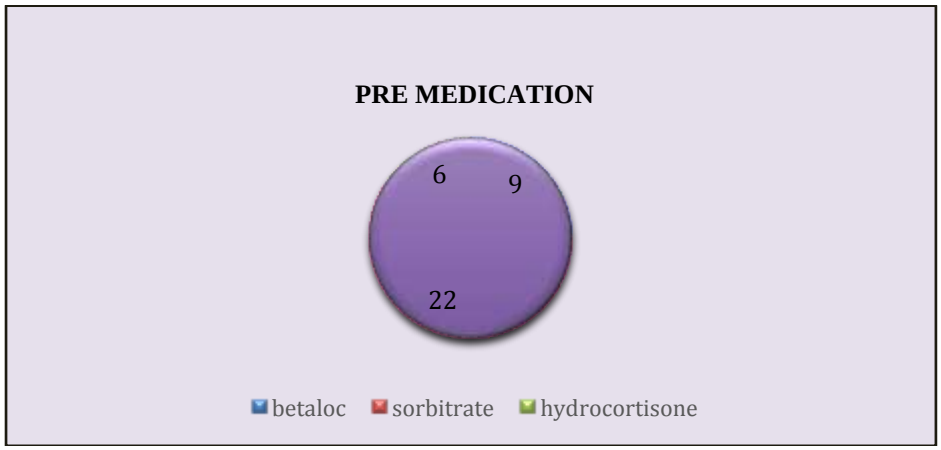

Figure-18: Out of all the patients, a total of 37 patients were at risk of adverse reactions to radiocontrast. Premedication was given to minimize the risk of adverse drug reactions.

IV. DISCUSSION –

We have conducted this study to determine the causality and severity of adverse drug reactions with the use of radiocontrast media as well as to identify risk factors for the occurrence of Hypersensitivity reactions and preventive measures for it.

In this observational study, a total of 113 patients were considered out of 300 patients who had undergone CECT, based on the inclusion and exclusion criteria. All the patients were assessed and counselled.

Out of 113 patients who experienced ADRs, 77 (68%) were found to be males, and 36 (32%) were found to be females. The current observation is consistent with the study by Singh et al[4] that found more frequent ADRs in males than females. Similar findings were found in a 1 year research by Bhowmick et al.[10]

The majority of patients with ADR were found to be under the age group (40-59) years of age. This contradicts the study by Bhoumivk et al[10], that found patients of age group 25-34 faced more adverse reactions than the others.

Similar to our study, which found that 94% of adverse drug reactions (ADRs) happened in patients receiving more than 70ml of contrast, Bhoumick et al.'s[10] study found that 70% of severe reactions happened in patients receiving higher iodine doses for CT angiography. The average median dose of 70ml of CM was the cause of the reactions.

Based on the CTCAE Severity scale used in our study, (96%) of the adverse reactions were classified as Grade 1 and (3.5%) as Grade 3 and no severe reactions. This is in accordance with the Singh et al.[4] study. The aforementioned observations make it clear that using LOCM and nonionic compounds is substantially safer. Another study by Patel et al[21] showed majority of reactions were moderate in nature and none were severe.

In the study, all 113 patients (i.e., 100%) experienced immediate reactions which were mild in nature. This observation bears similarities to the study carried out by Martin et al.[5]

The WHO scale displayed all cases as "probable" while the Causality assessment of ADRs done using Naranjo's Algorithm scale, had a score of '4' which denoted it is "possible" in nature, for all cases, which means drug as well as other causes could be responsible for the event. This is consistent with the research by Bhowmick et al[10] that found all ADRs were reported to be "possible" and it contrasts with the study by Singh et al[4] where 7 out of 8 cases were "probable" in nature, signifying drug is likely the cause of the event.

The lack of cutaneous adverse effects in our study was a surprising finding in comparison to others. We were only able to record symptoms that, for the most part, involved warmth. This may be due to the small number of participants we included in the study as well as the low occurrence of adverse drug reactions (ADRs) associated with the usage of non-ionic LOCM.

Despite adequate premedication, 32.3% of patients experienced breakthrough responses, according to a 2019 study by Min Jae Cha et al[6] However, in our study, the premedication given to all high-risk patients proved to be successful, comparable to another study by Jung Hyun Kim[8] (2021) where the majority of patients responded well to pharmacological prophylaxis with steroids and/or antihistamines, with a small number of

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2212-2223 www.ijprajournal.com ISSN: 2456-4494

patients experiencing significant adverse responses. Nevertheless, there is currently no evidence-based, standardized premedication regimen for the DHR that has been shown to be effective.

Concerning limitations, our study has several. One of these concerns is the limited number and lack of follow-up of outpatients. Another is that, only one CM was examined because iohexol was administered to 99% of the study's participants. An additional constraint was that the study was carried out for a brief period and at a single centre.

V. CONCLUSION-

In conclusion, the frequency of all types of adverse reactions is significantly decreased by the use of non-ionic, low osmolar radiocontrast agents. The majority of these reactions were of immediate type. The pharmacological prevention provided to high-risk patients is another factor in preventing adverse reactions. Most patients recover from their reactions without the requirement of any long-term treatment and care. However, to fully understand delayed hypersensitivity reactions and the risk factors associated with them, large-scale studies with continuous data collection may still be necessary in the future. All radiocontrast administrators, including radiologists and radiographers, need to be knowledgeable about ADRs to carry out prompt interventions.

REFERENCES

[1]. Iodinated Contrast Media and Their Adverse Reactions. Jagdish Singh and Aditya Daftary https://doi.org/10.2967/jnmt.107.047621

[2]. Survey of Radiologists' Knowledge Regarding the Mangement of Severe Contrast Material-induced Allergic Reactions. Christopher B. Lightfoot, Roshan Joseph Abraham, Thomas Mammen, Mohamed Abdolell, Sandeep Kapur, Robert J. Abrahamhttps://doi.org/10.1148/radiol.2513081651

[3]. Side Effects of Radiographic Contrast Media: Pathogenesis, Risk Factors, and Prevention. Michele Andreucci, Richard Solomon, and Adis Tasanaronghttps://doi.org/10.1155/2014/741018

[4]. Assessment of the Radio-contrast Media-Induced Self-Reported Adverse Drug Reactions in a Tertiary Care Hospital of North India: A Prospective Study. Pushpinder Singh, Manraj Kaur Gill, Mandeep Kaur, Rajiv Mahajan, Manjot Kaur https://doi.org/10.4103%2Fijabmr.ijabmr_381_21

[5]. Immediate and nonimmediate reactions induced by contrast media: incidence, severity and risk factors. Martín Bedolla-Barajas, Dante D Hernández-Colín, Jaime Morales-Romero, and Carlos Serrano-Salinas. https://doi.org/10.5415/apallergy.2013.3.4.241

[6]. Hypersensitivity Reactions to Iodinated Contrast Media: A Multicenter Study of 196 081 Patients. Min Jae Cha, MD • Dong Yoon Kang, MD • Whal Lee, MD, PhD • Soon Ho Yoon, MD • Young Hun Choi, MD • Jun Soo Byun, MD, PhD • Jongmin Lee, MD, PhD • Yun-Hyeon Kim, MD, PhD • Ki Seok Choo, MD, PhD • Bum Sang Cho, MD • Kyung Nyeo Jeon, MD, PhD • Jae-Woo Jung, MD, PhD • Hye-Ryun Kang, MD, PhD https://doi.org/10.1148/radiol.2019190485

[7]. Intravenous Contrast Medium Administration and Scan Timing at CT: Considerations and Approaches. Kyongtae T. Bae, MD, PhD https://doi.org/10.1148/radiol.10090908

[8]. Pharmacological prevention of delayed hypersensitivity reactions caused by iodinated contrast media. Jung-Hyun Kim, Sang Il Choi, Yoon Jin Lee, Byung-Keun Kim, Heung-Woo Park, Sang-Heon Cho, Yoon-Seok Chang and Sae-Hoon Kim https://doi.org/10.1016/j.waojou.2021.100561

[9]. Immediate and Delayed Reactions to Radiocontrast Media: Is There an Allergic Mechanism? Knut Brockow https://doi.org/10.1016/j.iac.2009.04.001

[10]. A study on adverse drug reactions to non-ionic contrast medium in an Indian population: a 1-year experience. Subhrojyoti Bhowmick, Esha Bhat, Buddhadev Panja, Satarupa Mukherjee, Shreya Sikdar, Arnab Biswas, A. Bari Ejaz, Tapan K. Chatterjee http://www.ijbcp.com/index.php/ijbcp/article/view/1189

[11]. Computed tomography contrast media extravasation: treatment algorithm and immediate treatment by squeezing with multiple slit incisions. Sue Min Kim, Kyung Hoon Cook, Il Jae Lee, Dong Ha Park &

Myong Chul Park https://doi.org/10.1111/iwj.12628
[12]. Radiological contrast agents and radiopharmaceuticals. Manoranjan S. D'Souza, MD, PhD, Rachel Miguel, and Sidhartha D. Ray, PhD, FACN https://linkinghub.elsevier.com/retrieve/pii/S0378608020300076
[13]. Trends in Adverse Events After IV Administration of Contrast Media. Sachiko T. Cochran, Karen Bomyea, James W. Sayre. https://www.ajronline.org/doi/10.2214/ajr.176.6.1761385
[14]. Incidence and Severity of Acute Allergic-Like Reactions to IV Nonionic Iodinated Contrast Material in Children. Jonathan R. Dillman, Peter J. Strouse, James H. Ellis, Richard H. Cohan, Sophia C. Jan https://www.ajronline.org/doi/10.2214/AJR.06.1328
[15]. Hypersensitivity Reactions to Multiple Iodinated Contrast Media. Inmaculada Doña, Gador Bogas , Marı´a Salas , Almudena Testera, Esther Moreno , Jose Julio Laguna and Marı´a .Jose´Torres. https://www.frontiersin.org/article/10.3389/fphar.2020.575437/full
[16]. Diagnosis and Prevention of Hypersensitivity Reactions to Iodinated Contrast Media. Hye-Ryun Kang, Jiung Jeong, Knut Brockow https://e-aair.org/DOIx.php?id=10.4168/aair.2022.14.4.348
[17]. Evaluation of adverse reactions to contrast media in the hospital E-J KYUNG, J-H RYU and E-Y KIM http://www.birpublications.org/doi/10.1259/bjr.20130418
[18]. Contrast Media Reactions: Data Analysis and Hypothesis. Anthony F. Lalli, M.D http://pubs.rsna.org/doi/10.1148/radiology.134.1.6985735
[19]. Immediate Mild Reactions to CT with Iodinated Contrast Media: Strategy of Contrast Readministration without Corticosteroids. Sae-Jin Park, MD • Dong-Yoon Kang, MD • Kyoung-Hee Sohn, MD • Soon-Ho Yoon, MD • Whal Lee, MD, PhD • Young-Hun Choi, MD • Sang Heon Cho, MD, PhD • Hye-Ryun Kang, MD, PhD http://pubs.rsna.org/doi/10.1148/radiol.2018172524
[20]. Adverse reactions to ionic and nonionic contrast media. A report from the Japanese Committee on the Safety of Contrast Media. H Katayama, K Yamaguchi, T Kozuka, T Takashima, P Seez, K Matsuura. https://doi.org/10.1148/radiology.175.3.2343107
[21]. A study of adverse drug reactions to iodinated contrast agents in tertiary care teaching hospital. Dhara Patel, Ajita Pillai, Farah Kausar https://www.ijbcp.com/index.php/ijbcp/article/view/3645