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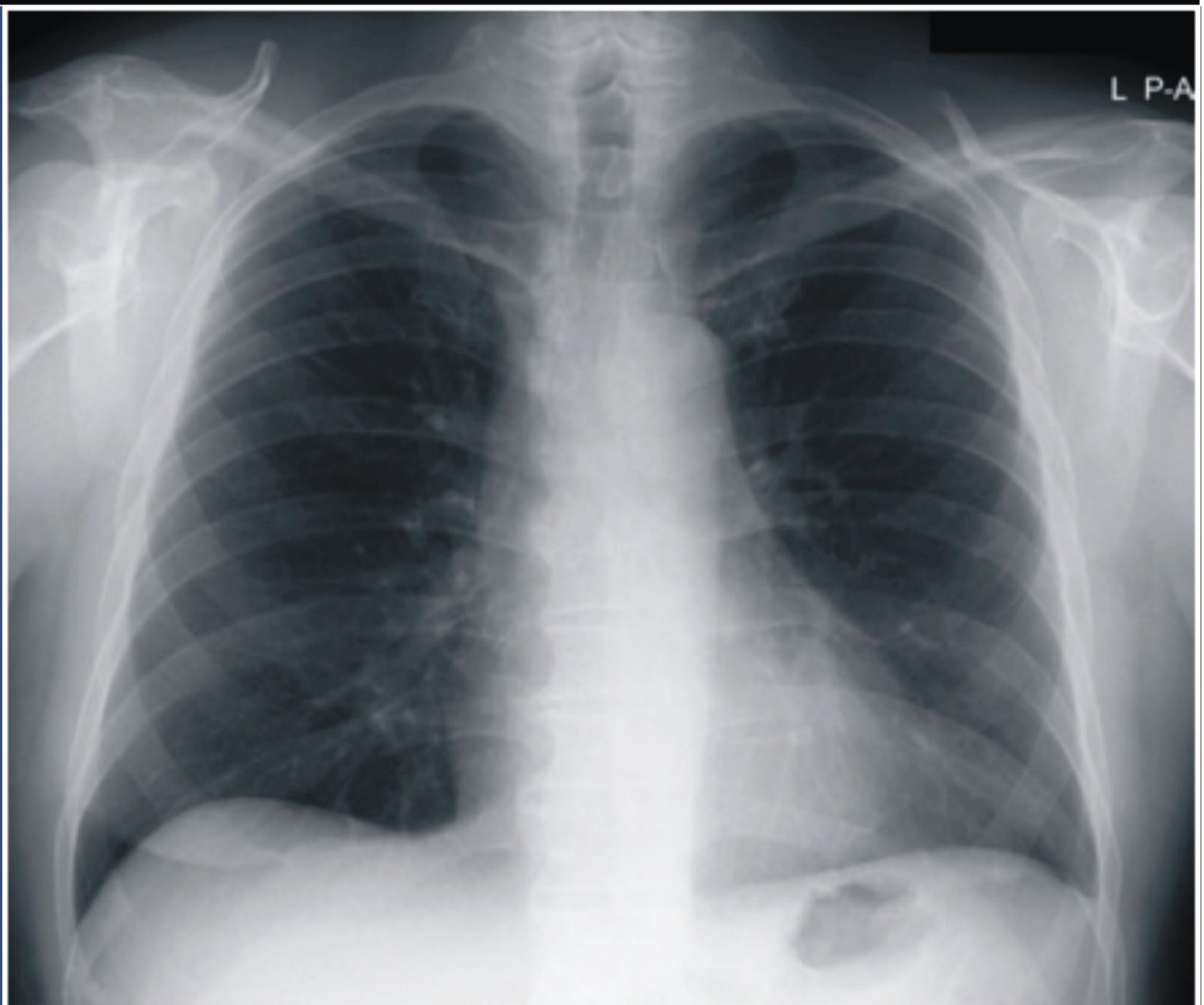


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# Hypersensitivity Reactions to Urografin (76%): A Pilot Study in Northeast Nigeria

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**ABSTRACT**

**Background**: Patients react to radiographic contrast media in diverse ways.
**Objectives:** To assess hypersensitivity reactions to Urografin contrast media among patients booked for contrast-enhanced computed tomography scans in a tertiary hospital in Nigeria.
**Methods**:A prospective, 30-minute observation of each of 30 patients who had administration of urografin 76% intravenously. They were observed from the point of administration to the end of the investigation. Observed clinical reactions were documented and results were presented in tables.
**Results***:* Out of thirty patients, six patients (20%) had nausea which is termed as mild reaction. Four of them (13.3%) vomited, a condition considered as moderate reaction. Twenty (66.7%) did not present with any reaction to contrast within the study time frame.
**Conclusion:** Nausea and vomiting were reactions observed in the study. No severe hypersensitivity reaction among all the patients who participated in the study was recorded.
**Keywords**: Computed tomography, contrast, hypersensitivity, nausea, Urografin

## Introduction

Computed tomography (CT) scan is an imaging procedure that uses special x-ray equipment to create detailed pictures, or cross-sectional scans, of areas inside the body[1, 2]. During some CT examinations, patients will be required to take a special contrast agent (orally, rectally or via injection) to make specific organs, blood vessels and, or tissues "stand out" with more image contrast to better show the presence of disease or injury [1-4]. Thus CT contrast media are substances which highlight specific areas of the resultant CT image [3].

Urografin is an ionic radio-contrast agent which contains the active ingredient sodium diatrizoate – meglumine diatrizoate. In radiology, the overall incidence of severe acute reactions to intravenous contrast administration depends on the class of agent administered. Specifically, Severe acute reactions are 5 times more common after the administration of an ionic, monomeric, high-osmolarity agent as against low- or iso-osmolar agent with a risk of 0.22% to 0.04% [3, 5]. Overall mortality from acute reactions to intravenous contrast agents is 1:13,000 to 1:169,000 [2, 5-7].

A previous study has found minor and acute side effects from administration of contrast media, and with the latter classified as mild, moderate, and severe. Also, it has been found that although, contrast media have evolved from ionic, high-osmolality to non-ionic, the availability and cost of non-ionic contrast remains an issue [3, 8]. As a result of this challenge, some radiodiagnostic centres still use ionic contrast agents for certain radiological investigations. In this study, we focussed on hypersensitivity reactions from the administration of Urografin 76% during CT scans.

Because contrast media have no therapeutic effect, the ideal agents should provide optimal quality without substantial adverse effects [9, 10].Unfortunately, adverse reactions to iodinated contrast agents are common [9]. In fact, reports in the literature stated that symptoms of an adverse reaction to intravenous iodinated contrast agents were diverse ranging, and sometimes serious, especially because most patients that present for CT scan have underlying pathological conditions [9, 11].

Generally, drugs and other chemical substances such as intravenous contrast agents react differently in different people due to certain morphological/physiological variations, co-mobidities, socio-economic and demographic differences in patients [12].With over 75 million contrast-requiring procedures performed annually, it is important to understand the risk factors, pathogenesis, diagnosis, prevention, and treatment of adverse reactions caused by iodinated contrast media (ICM) [13].

Iodinated contrast media are among the most commonly prescribed medications in the history of modern medicine, with approximately 80 million doses administered worldwide corresponding to approximately 8 million litres [10, 14]. The hypersensitivity reactions to contrast media are immunoglobulin E (IgE) and non-immunoglobulin E (non-IgE-mediated anaphylaxis), with activation of mast cells, coagulation, kinin and complement mechanisms, inhibition of enzymes, and platelet aggregation [15].Mild hypersensitivity reactions (incidence < 3%) consist of immediate skin rashes, rhinorrhea, nausea, brief retching, and/or diaphoresis, coughing and dizziness; moderate to severe (incidence <0.04%) reactions include persistent vomiting, pruritus, diffuse urticaria, headache, facial edema, laryngeal edema, dyspnea, palpitations, tachycardia or bradycardia, abdominal cramps, angioedema, coronary artery spasm, hypertension or hypotension, life-threatening cardiac arrhythmias (i.e. ventricular tachycardia), overt bronchospasm, laryngeal edema, cardiac failure and loss of consciousness, pulmonary edema, seizures, syncope. Mortality is less than one death per 100,000 patients [15].

In our locality, there is dearth of empirical evidence regarding hypersensitivity to contrast media. Consequently, the primary objective of this study was to document hypersensitivity reactions from intravenous urografin 76% utilized for patients booked for contrast enhanced CT Scans at Specialist Hospital, Bauchi, Nigeria.

## Material and method

A prospective cross-sectional study which was undertaken between 1st August to 31st December, 2016. Patients who were booked for CT scans and had IV contrast administered were included in the study. All patients who participated indicated that they had no previous reaction to contrast agents. The patients were observed for 30 minutes following administration of urografin 76%. The observation was carried out by a team comprising a radiologist, two radiographers and one nurse. All reactions which were observed throughout the process were documented. Ethical clearance was obtained from the research ethics committee of the institution.

## Study Endpoints

*Mild hypersensitivity reaction*: nausea
*Moderate Hypersensitivity reaction*: Vomiting, pruritus
*Severe Hypersensitivity reaction*: Urtricaria, death

**Procedure**

A total of 3 paediatric and 27 adult patients (18 males and 12 female) with age range of 1 – 79 years were included in the study. After interviewing patients for history of hypersensitivity reactions, they were positioned supine on the CT couch and contrast was injected via the antecubital vein using an automatic CT contrast injector (3.5mls/s). A range of 10 – 60 mls of urografin 76% volume was administered based on age and clinical indication. Finally, patients were carefully examined for hypersensitivity reaction from the time of injection till the end of the procedure. Data were manually tabulated.

**Results**

Mean age of patients was 44 years. Reactions were observed in ten patients (33.3%) with six appearing mild and four being moderate. Vomiting was the common reaction amongst the moderate group. These are all summarized in Tables 1 and 2.

**Discussion**

Thirty patients already booked for CT scans and required contrast administration to outline certain structures were observed carefully to determine if any abnormal reaction occurred due to the Urografin 76% contrast agent. Allergic history to contrast agents, urticaria, history of previous allergy to drugs other than contrast agents, contrast agent concentration > 70%, age <50 years old, and a total contrast agent dose >65 g were identified as predictors for adverse reactions to contrast agent in a study by Kobayashi et al. [13] Even though these predictions were based on low osmolar non-ionic contrast agents, the results proved beneficial in this study as patients who vomited continuously claimed to have had allergy to previous drugs in the past. This study was monitored by a radiologist,two radiographersand a nurse at a tertiary healthcare institution in Nigeria.

**Table 1. Demographics Information of Patients**

| Patient | Age (year) | Gender | Volume of contrast (ml) | Adverse reactions observed | |
|---|---|---|---|---|---|
| | | | | Nausea | Vomiting |
| **1** | 74 | M | 60 | * | * |
| **2** | 28 | M | 60 | * | - |
| **3** | 31 | M | 60 | * | - |
| **4** | 1 | F | 10 | - | - |
| **5** | 3 | M | 60 | - | - |
| **6** | 41 | M | 20 | - | - |
| **7** | 41 | F | 40 | - | - |
| **8** | 35 | M | 60 | - | - |
| **9** | 38 | M | 60 | - | - |
| **10** | 48 | F | 40 | - | - |
| **11** | 70 | F | 60 | - | - |
| **12** | 70 | F | 60 | - | - |
| **13** | 45 | M | 45 | - | - |
| **14** | 40 | F | 60 | - | - |
| **15** | 34 | F | 40 | - | - |
| **16** | 25 | M | 40 | - | - |
| **17** | 70 | M | 60 | - | * |
| **18** | 71 | M | 20 | - | - |
| **19** | 75 | F | 60 | - | - |
| **20** | 42 | M | 60 | - | - |
| **21** | 25 | F | 40 | - | - |
| **22** | 37 | M | 20 | - | * |
| **23** | 45 | M | 20 | * | - |
| **24** | 40 | F | 20 | - | - |
| **25** | 79 | M | 40 | - | - |
| **26** | 33 | M | 40 | - | - |
| **27** | 72 | F | 40 | * | - |
| **28** | 22 | F | 45 | * | - |
| **29** | 45 | M | 60 | - | - |
| **30** | 36 | M | 40 | - | * |
| **Mean** | 44 | | 44.7 | | |

In this study, six patients (20%) had nausea due to the contrast and four of the patients (13.3%) vomited as a result of the contrast. However, twenty (66.7%) indicated that they did not feel any abnormal reaction from the time of administration of the contrast until the end of the examination.

In a prospective study comparing a group of patients undergoing computed tomography (CT) with iohexol and another group undergoing CT without contrast media, delayed cutaneous adverse reactions were significantly more frequent in the iohexol group (14.3%) than in the control group (2.5%) [16]. Similarly, in two prospective studies there was a significantly higher rate of rash following the intra-arterial utilization of iodixanol (Visipaque 320, 12.2%, and 10.4%) than with either the monomer iopamidol (Niopam 300) or the ionic dimer ioxaglate (Hexabrix) (2.7%–4.2%)[17, 18]. In this study however, none of the patients presented with pruritus or urticaria.

Another recent analysis including 36 randomized controlled trials for a total of 7,166 patients (3672) patients receiving the iso-osmolarcontrast medium(IOCM) iodixanol and 3494 patients receiving other low osmolar contrast media (LOCMs) showed contrast induced nephropathy incidence for iodixanol not statistically different from the pooled low osmolar Contrast (LOCM); a significant reduction of contrast induced nephropathy with iodixanol was only observed in direct comparison of iodixanol with the LOCM iohexol. [19, 20]. This suggests that there are differences among low-osmolar contrast media (LOCM) such that each molecule should be considered individually.

## Conclusion

Urografin 76% is an ionic contrast agent that is safe for use in computed tomography contrast study. No severe hypersensitivity to the contrast agent was observed in this small-scale feasibility study.

## Limitation

The major limitation of this study was the inability to follow patients in their homes for any post examination adverse reaction (delayed, non-acute reactions) which may be due to the Urografin 76%. Nevertheless, this study has provided information on immediate hypersensitivity reactions to the Urografin 76% contrast agent. In the future we shall conduct a larger and more extensive study.

## Competing Interests

The authors declare that they have no competing interests.

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