

Evaluation of Adverse Drug Reactions (ADRS) Among In-Patients Admitted into the Adult Medical Wards of a Tertiary Hospital in Nigeria

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ABSTRACT

Adverse drug reactions (ADRs) are considered as a major health problem among hospitalized patients. The safety of many drugs currently in use clinically has been studied. However, their safety profiles may not necessarily be universally applicable due to local environmental and genetic influences resulting in differences in the incidence, pattern and severity of ADRs. The objective of this study was to determine the magnitude and pattern of ADR events in the adult medical wards of the University of Ilorin Teaching Hospital (UITH). A prospective descriptive study was conducted over a period of one year on all admissions in the adult medical wards of the UITH. Data were extracted from daily ADRs reports from March 2013 to February 2014. Extracted data were analyzed descriptively using SPSS version 20. A total of 2012 patients consisting of 910 males and 1102 females were admitted to, and assessed in the wards. Fifty two (2.58%) patients with ADRs were detected and reported. 57.7% of reported ADRs cases were patients admitted specifically due to an ADR and 42.3% occurred while on admission. Mostly implicated classes of drugs were anti-inflammatory/analgesics (21.2%) and antidiabetics (15.4%). The most commonly affected organ system was the central nervous system (40.4%). A pattern of ADRs in adults was established and the magnitude for different drug classes was determined. A need to establish a regular reporting program, assessment of knowledge levels of health workers, and incorporation of molecular methods to define/determine responsible allergens is also necessary to enhance safety in drug use.

KEY WORDS: Adverse drug reactions, pharmacovigilance, hypersensitivity reaction, allergic patients

INTRODUCTION:

Adverse drug reactions (ADRs) are common multi-organ clinical problems accounting for 2 - 6% of all hospital admissions ^[1-4]. ADRs could lead to extended hospitalisation, outright withdrawal of offending agents from circulation and ultimately contribute significantly to an increase in healthcare costs. Adverse drug reactions have been found to have a direct effect on healthcare costs accounting for 9.5% of such in a study population ^[5]. Also, the impact and management of ADRs in the USA has been estimated to be up to 30.1 billion dollars annually^[6]. The clinical impact of ADRs has thus necessitated the development of ADR monitoring and reporting systems collectively referred to as pharmacovigilance.

An adverse reaction can occur with any class of drug. Several classes including the beta lactams,^[7, 8] the non-steroidal anti-inflammatory agents^[9, 10],

and anti-seizure drugs ^[11-13] are associated with a high incidence of ADRs. Beta-lactam antibiotics have been recognized as the most frequent cause of immunological reactions ^[14]. In addition to the above mentioned drugs, the use of herbal medicinal products has increased remarkably over the past few years. Self-medication of these herbal products, high cost of modern drugs and lax regulatory protocols governing the use of herbals has made them promising candidates for ADRs ^[15]. Epidemiologic data regarding the prevalence of drug allergies suggests a varied prevalence among different populations, which could be attributed primarily to the different criteria for inclusion and methodologies employed ^[16]. Majority of the studies conducted on adverse drug reactions in Nigeria and Sub Saharan Africa have been via the collection of data using questionnaires ^[17-20] to try and define various patterns of ADR occurrence. This study, to our knowledge is the first of its kind

in the north-central Nigeria geographic region that aimed to detect, and quantify the frequency of ADRs in adult medical in-patients in a tertiary hospital. The long term goal of this study is to generate information on the prevalence of ADRs as a precursor for further studies in this less studied geographical region. The outcomes of which will enhance the accuracy of ADR monitoring and reporting and ultimately the safety of these drugs.

MATERIALS AND METHODS:

A one year prospective study was conducted over a period of one year in both adult male and female medical wards and the medical emergency ward,

of the University of Ilorin Teaching Hospital (UITH) Nigeria. A study specific 29 item questionnaire (Appendix 1) was used to collect ADR information for consenting patients. This questionnaire was completed for all patients at admission. They were subsequently evaluated on daily basis until their discharge. Evaluation comprised examination of medical records, review of prescription charts, and patient interviews. All forms of ADRs were included in this study. Data were then extracted from daily ADRs reports from March 2013 to February 2014 retrospectively. The extracted data were analyzed descriptively using SPSS version 16.0 for descriptive statistical analysis.

RESULTS

Table 1: Baseline characteristics of patients assessed in the adult medical ward.

Hypersensitivity characteristics of patients		
	Frequency	%
Tolerant patients	1960	97
Hypersensitive patients	52	3
Sex characteristics of hypersensitive patients		
	Frequency	%
Male	25	48
Female	27	52
Characteristics of patients with hypersensitivity reactions (n = 2012)		
Age distribution of patients	Frequency	%
11-20	160	7.9
21-30	432	21.5
31-40	344	17.1
41-50	320	16
51-60	364	18.1
61-70	332	16.5
>70	60	2.9
Characteristics of patients with hypersensitivity reactions (n = 52)		
Age distribution of patients	Frequency	%
11-20	3	5.8
21-30	10	19.2
31-40	7	13.5
41-50	12	23.1
51-60	6	11.5
61-70	9	17.3
>70	5	9.6

The patients demographic data including sex, age distribution, and occupation and also the total frequency of occurrence of ADRs in patients ($n = 2012$) was assessed.

2012 patients comprising 910 male and 1102 females were admitted into the medical wards in the period under review. Eight hundred and thirty seven (837) patients were admitted into the male

and female medical wards while 1175 were admitted into the emergency wards. Fifty two patients were determined to have developed an adverse drug reaction 52% of whom were female. Of these patients 21 (40.4%) were admitted and transferred to the wards while 31 patients were admitted to the emergency unit. The age distribution of ADR occurrence in allergic patients

showed the frequency (%) of susceptible patients from 11-20 to >70 years. The peak occurrence (highest frequency) of ADRs within patients was observed at 41 – 50 years.

Table 2: Onset of ADRs and determined causes in hospitalized patients. The time of adverse drug reactions their identifiable causes and classes of implicated drugs were assessed in all hypersensitive patients

Time of Adverse drug reactions (n = 52)	
	%
Before admission	59
During admission	41

Cause of Adverse drug reactions (n = 52)	
	%
Physician prescription error	11
Verification error	14
Overdosage	25
Other causes	50

Class of drugs implicated in Adverse drug reactions			
Class of drug	No. of patients (n = 2012)	No. of ADR reported	%
NSAIDS	200	12	6.0
Antihypertensive	465	5	1.1
Antidiabetic	200	6	3.0
Antibiotics	625	4	0.6
Antiretroviral	200	2	1.0
Antipsychotic	160	4	2.5
Herbal	20	3	15.0
Anti-snake venom	10	4	40.0
Corticosteroids	80	2	2.5
Antimalarial	20	1	5.0
Others	32	9	28.1

The time of adverse drug reactions and their identifiable causes were assessed in all hypersensitive patients ($n = 52$). The classes of drugs used in all patients ($n = 2012$) and the frequency implicated in the elicitation of these reactions were also determined. The time of onset of ADRs in 52 drug hypersensitive patients was assessed. 41% of these reactions were the reason for patient hospitalization while 59% of these reactions developed during their hospital stay

(during admission). Physician prescription errors, verification errors and overdosage were the main reasons identified for the development of ADRs in this group of patients. The frequency of drugs implicated in the elicitation of ADRs were in the order of Anti-snake venom > Herbals > NSAIDs > Antimalarial > Antidiabetics > antipsychotics/corticosteroids.

Table 3: Specific organ systems affected by the manifestation of adverse drug reactions

Affected systems	Number of patients	
	involved (<i>n</i> = 52)	%
Gastrointestinal tract & liver	13	25
Cardiovascular system	7	13
Central nervous system	23	44
Respiratory system	4	8
Dermatology	2	4
Haematology	2	4
Renal	1	2

Organs and systems affected in the cohort of drug allergic patients (*n* = 52) were determined and the frequencies of occurrence assessed. The central nervous system (44%), gastrointestinal tract (23%), cardiovascular system (13%) and the respiratory system (7%) were all implicated. The frequency of ADRs occurring in specific organs in this cohort of allergic patients indicated that the skin (*n* = 2), blood (*n* = 2), the liver (*n* = 1), and the kidney (*n* = 1) were directly involved in the elicitation of these reactions.

Table IV: Adverse Drug Reaction management strategies and outcomes in drug hypersensitive patients

Management strategies		
	%	
Non-pharmacologic treatment	43	
Transfusion	4	
Dose reduction	4	
Stoppage of drug	27	
Others	8	
Pharmacologic (Drug) treatment	57	
Outcomes of management		
	No. of patients	%
Full recovery	49	94.2
Recovery with disability	2	3.8
Death	1	1.9

The management strategies employed in the attempt to resolve ADRs and resultant outcomes were determined in the cohort of allergic patients (*n* = 52). 57% of cases required drug treatment. Non-pharmacologic treatment employed included transfusion, dosage reduction, drug withdrawal and other forms of management made up the balance. Discontinuing the offending agent presented the

largest modality employed for the non-drug control of ADRs. Forty-nine patients representing 94.2% of allergic patients recovered fully, though nine of these patients required a prolonged hospital stay. Two patients (3.8%) recovered with a form of disability and one death was recorded representing 1.9%.

DISCUSSION

Drug management of a host of clinical conditions may involve the concurrent use of multiple drugs^[21] which may be associated with the development of ADRs. As the frequency of ADR has been related to the number of drugs administered^[22]. The assessment of ADRs using prospective studies has been attempted in various racial and age groups^[23-25]. In the present study conducted over a period of one year (February 2013 – March 2014) the magnitude and pattern of ADR events was studied in a population of adult patients admitted into the adult wards in UITH. A wide range of drugs were implicated coupled with multiple end organ system effects and outcomes. From the total number of patients ($n = 2012$) assessed 52 (2.58%) developed adverse drug reactions either prior to, or during hospital admission. Higher frequencies of ADRs have been recorded in other studies^[26] which could be due to the inclusion of other criteria such as anticancer and antitubercular drugs which produces high incidences including up to 80% in patients undergoing chemotherapy^[23]. This has the potential to alter overall population statistics. These patients were found to develop significant ADRs to over 10 specific classes of drugs. Most drugs implicated in the ADRs observed in our study have been established previously. Studies have shown a high frequency of reactions in response to NSAIDs^[27-29], herbals^[30, 31], antimalarials and anti-snake venom^[17, 32-34] pattern that has also been captured in our study. Sex differences play a role in the action of many drugs and have been implicated in the severity and frequency of ADRs to antiretroviral agents, colchicine and metabolism of benzodiazepines^[35-38]. In this study a small difference was observed as 52% of all adverse reactions were observed in women a pattern consistent with previous studies conducted in Western Europe^[39, 40]. The manifestations of ADRs occur both prior to and post hospitalization with 41% of these admissions due specifically to the occurrence of these reactions. The limitations of this study meant that the idiosyncratic nature of these reactions largely due to involvement of various molecular

mechanisms could not be fully explored. Thus, directly observed clinical indices such as the wrong use of medicaments influenced by factors such as physician errors, overdose and verification errors were the only factors that could be fully confirmed. Majority of adverse effects manifested in the central nervous system, gastrointestinal tract and cardiovascular system in that order, regions that have been implicated previously though not in that particular order^[41, 42] specific end organ involvement in the skin, blood, kidneys and liver were also manifested. Though age is not an independent risk factor of adverse drug reactions^[43], the frequency of occurrence in patients between the age of 41 – 50 years was higher than in other groups studied. Management strategies employed both drug treatment and non-drug measures playing a major role in the final outcomes observed. Majority (94.2%) of allergic patients had a full recovery with a few recovering with disability. The death recorded was due to the pre-existing pathology and not the ADR. While it was possible to detect ADRs with this study, obvious limitations such as the absence of protocols to enable us determine the influence of race, phenotype and specific proteins presented us with difficulties. Thus, in the attempt to characterise ADR patterns in hospitalized patients it is clear that the analysis of the molecular mechanisms is essential for a full elucidation. This is due to the number of reactions which did not have a verifiable aetiology (due to other causes). The high frequency of ADRs to herbal preparations and anti-snake venom are areas that should be further looked into especially when the high rate of herbal preparations consumption is considered. This is also necessary to eliminate the possibility of a bias arising due to differences in population size when compared with studies involving other drugs.

To conclude, our data shows a pattern of adverse reactions to various drug formulations in adult in-patients, the magnitude of which should be of concern to all. How these reactions arise due to cellular interactions still remain to be defined.

NOTES

The authors declare no competing financial interest.

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