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# TO EVALUATE THE INCIDENCE AND CHARACTERISTICS OF CONSUMER ADVERSE DRUG REACTION REPORTING HOSPITALIZATION

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## ABSTRACT

The direct reporting of adverse drug reactions by patients is becoming an increasingly important topic for discussion in the hospital of Pharmacovigilance. Voluntary adverse drug reaction (ADR) reporting is fundamental to medical drug safety surveillance; however, substantial under-reporting exists and is the main limitation of the system. At this time, hospital accepts consumer reports. We present an overview of experiences with consumer reporting in various hospital of the hospital. The potential contribution of patient reports of adverse drug reactions is discussed, both in terms of their qualitative and quantitative contribution. The crucial question is one of whether patient reports will increase the number and qualities of the reports submitted or lead to a more timely detection of signals of possible adverse reactions, thus contributing to an enhancement of the existing methods of drug safety monitoring. To date, the data available are insufficient to establish such added value.

**KEYWORDS:-** Adverse drug reactions, Pharmacovigilance, consumer reports, reporting system, patients report, spontaneous reporting systems, WHO Adverse Reactions, Pharmacovigilance.

## BACKGROUND

The incidence of adverse drug reaction (ADR)-related hospitalizations has usually been assessed within hospitals. Because of the variability in results and methodology, it is difficult to extrapolate these results to a national level and adverse drug reactions (ADRs) are an important public health problem, representing a major cause of morbidity and mortality. However, several hospital or wards have no recent studies available.

Adverse reactions involving the skin and mucous membranes, central nervous system, musculoskeletal system, pregnancy, and eyes were most commonly reported. Severe headache was the most frequently reported adverse reaction. In four cases headaches were attributed to pseudo tumor cerebral. Some of the reported reactions, for example, a disulfiram (Ant abuse)-like reaction and oculogyric crisis, have not been described previously in the literature. Other reports, such as congenital malformations, serve to emphasize sorne of the serious reactions that are known to occur. These spontaneous reports of adverse reactions associated with isotretinoin use, together with the literature we review, may help alert physicians to the diverse spectrum of adverse reactions that may develop in patients taking isotretinoin.

**AIM (OBJECTIVES):-** To evaluate the incidence and characteristics of consumer adverse drug reaction reporting hospitalization.

## INTRODUCTION

The World Health Organization's (WHO) stated definition of an adverse drug reaction (ADR) is 'A response to a drug which is noxious, and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function'. The adverse drug reaction (ADR) is an injury caused by taking medications they Define an adverse drug reaction as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, warrants prevention or specific treatment, administration and alteration of the dosage regimen. ADRs may occur following a single dose or prolonged administration of a drug or result from the combination of two or more drugs. The meaning of this term differs from the term "side effect" because side effects can be beneficial as well as detrimental.[1,2]

Examples of such adverse drug reactions include rashes, peripheral neuropathy, constipations, increased sleepiness, gassiness, episodes, jaundice, and anemia, a decrease in the white blood cell count, kidney damage, and nerve injury that may impair vision or hearing.

These reactions tend to be more serious but typically occur in a very small number of people.[1,3,4]

**CLASSIFICATIONS OF ADVERSE DRUG REACTION (ADR):-** Adverse drug reaction (ADR) may be classified by e.g. cause and severity (Seriousness).

❖ **CAUSE**

1) **Type A: -** Augmented pharmacologic effects - dose dependent and predictable. Usually a consequence of the drug's primary pharmacological effect or a low therapeutic index of the drug like nausea from dioxins, and they are therefore predictable. Such reactions are usually due to inappropriate dosage, especially when drug elimination is impaired. The term 'side effects' is often applied to minor type a reactions.[1,2,4]

2) **Type B: -** Idiosyncratic.

❖ **SEVERITY (SERIOUSNESS)**

The Food and Drug Administration defines a serious adverse event as one when the patient outcome, relevant medical, suspected medicine or concomitant medical products including self medication and herbal remedies with therapy dates.[1,5,8]

- Death
- Life-threatening
- Hospitalization (initial or prolonged)
- Disability - significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.
- Congenital abnormality
- Requires intervention to prevent permanent impairment or damage

Severity is a point on an arbitrary scale of intensity of the adverse event in question. The terms "severe" and "serious", when applied to adverse events, are technically very different. They are easily confused but cannot be used interchangeably, requiring care in usage.[5,9]

A headache is severe if it causes intense pain. There are scales like "visual analog scale" that help clinicians assess the severity. On the other hand, a headache is not usually serious (but may be in case of subarachnoid hemorrhage, subdural bleed, even a migraine may temporally fit criteria), unless it also satisfies the criteria for seriousness listed above.[9,10,11]


Fig: - Division of ADRs based on gender of the patients.


Fig: - Division of ADRs based on Age Group of the patients.

**SIGNS AND SYMPTOMS OF AN ADVERSE DRUG REACTION**

- Mild symptoms include red, itchy, flaky, or swollen skin.
- Severe symptoms include skin that blisters or peels, vision problems, and severe swelling or itching.
- Anaphylaxis symptoms include throat tightness, trouble breathing, tingling, dizziness, and wheezing.

**DIAGNOSING ADVERSE DRUG REACTION (ADR):-** The diagnosis of ADRs is highly subjective and imprecise. Complaints such as fatigue, inability to concentrate, and excessive sleepiness have been reported by healthy individuals not taking medications. It is also well known that patients receiving a placebo report ADRs.[25] However, drugs as disease and symptom producing agents should always be considered in the formulation of a differential diagnosis and the following step-wise process can be helpful in assessing possible drug-related adverse reactions.

- Step 1 – Identify the drug(s) taken by the patient.
- Step 2 – Verify that the onset of signs and symptoms was after the initiation of pharmacological intervention.
- Step 3 – Determine the time-interval between the initiation of drug therapy and the onset of signs and symptoms.
- Step 4 – Stop drug therapy and monitor signs and symptoms.
- Step 5 – In rare instances it may be appropriate to restart drug therapy and monitor for recurrence of signs and symptoms.

**ADVERSE REACTIONS TERMINOLOGY: -** The WHO Adverse Reactions Terminology (WHOART) is a dictionary meant to serve as a basis for rational coding of adverse reaction terms. The system is maintained by the Uppsala Monitoring Centre (UMC), the **World Health Organization** Collaborating Centre for International Drug Monitoring.[12,22,25]

**CONSIDERED THE COMMON SIDE EFFECTS:-** Common side effects include upset stomach, etching, reassess, nausea, vomiting, dry mouth, and drowsiness. A side effect is considered serious if the result is: death, life-threatening, hospitalization, disability, requires intervention to prevent permanent impairment or damage Permanent damage and exposure prior to conception or during pregnancy caused birth defect.[14,16]

Our study highlights clearly that valuable differences between ADR reports from patients and reports from healthcare professionals exist. Differences in interpretation by patients and healthcare professionals may cause the observed disparities in seriousness and outcome of reported ADRs. However, the similarities between patient reports and reports from healthcare professionals in most frequently reported ADRs and most frequently reported drugs are strike. [16,17,19]

**PHARMACOLOGICAL INVESTIGATION**

❖ **Reactions that may occur in anyone**

- Drug overdose—Toxic reactions linked to excess dose or impaired excretion, or to both.
- Drug side effect—Undesirable pharmacological effect at recommended doses.
- Drug interaction—Action of a drug on the effectiveness or toxicity of another drug.

❖ **Reactions that occur only in susceptible subjects**

- Drug intolerance—A low threshold to the normal pharmacological action of a drug.
- Drug idiosyncrasy—A genetically determined, qualitatively abnormal reaction to a drug related to a metabolic or enzyme deficiency.
- Drug allergy—An immunologically mediated reaction, characterized by specificity, transferability by antibodies or lymphocytes, and recurrence on re-exposure.
- Pseudo allergic reaction—A reaction with the same clinical manifestations as an allergic reaction (eg, as a result of histamine release) but lacking immunological specificity.

❖ **Expected reactions**

- Extensions of therapeutic effect.
- Undesirable side-effects.
- Interactions with other drugs.

❖ **Unexpected Reactions**

- Anaphylaxis.
- Allergic reactions.
- Prescription error.
- Administration errors.
- Idiosyncratic metabolism reactions, leading to increased or decreased clearance.
- Interaction with the critical care environment.

**MECHANISMS OF ADRs :-** As research better explains the biochemistry of drug use, fewer ADRs are Type B and more are Type A. Common mechanisms are.

❖ **Abnormal pharmacokinetics due to**

- genetic factors
- co morbid disease states

❖ **Synergistic effects between either**

- a drug and a disease
- two drugs

❖ **Antagonism effects between either**

- a drug and a disease
- two drugs.

**METHODS**

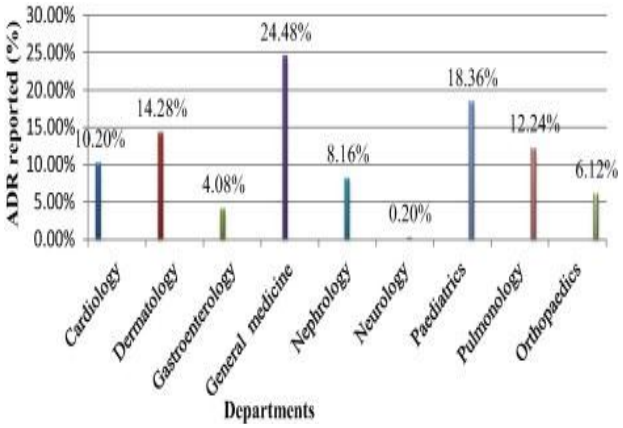
We conducted a nationwide study of all hospital admissions in 2021. Data were retrieved from a hospital discharge records. Demographic, clinical, and pharmacological data on patients admitted to nine wards of Internal Medicine, from 2019 to 2021, were collected by trained, qualified monitors, who screened all medical records. The rate of ADRs occurred during hospital stay and those leading to hospitalization were analyzed. A descriptive analysis of the reactions, suspected drugs, and associated factors was performed according to the setting analyzed. All acute, non-planned admissions to all Dutch academic and general hospitals in 2021 were included in the study (n = 668 714). From these admissions we selected all hospitalizations that were coded as drug-related, but intended forms of overdose, errors in administration and therapeutic failures were excluded. Hence, we extracted all ADR-related hospitalizations. [22,25,29] We compared age, sex, relevant medical, seriousness of the reactions, outcome, suspected medicine, concomitant medicine and the risk of a fatal outcome between patients admitted with ADRs and patients admitted for other reasons, as well as the most frequent main diagnoses in ADR-related hospitalizations and which drugs most frequently caused the ADRs. In addition, we evaluated to what extent these ADRs were reported to the Netherlands Pharmacovigilance Centre Lareb for spontaneous ADR reporting.[30,31,35]

**DATA COLLECTION:-** All patients admitted to participating hospitals during the 2-3 years were included in the study and followed until discharge. Patients were excluded if they were discharged within 24 hours and had been transferred from other hospitals or other wards within the study hospitals. Data collected included sociodemographic characteristics, previous medical history, admission and discharge diagnoses, length of stay, laboratory tests, instrumental procedures, therapies administered (before admission and during hospital stay), medications prescribed at discharge, as well as information on the dosage, frequency, route, and indication of use of drugs. Data collected were entered into a computerized database developed. Based on the collected data, all patients were classified into three different groups depending on whether they have developed at least one ADR (patients with ADR occurring during hospitalization and patients with ADRs that caused hospitalization) or not (patients without ADR).[34,35,36]

All identified cases of ADRs were reviewed by a research team consisting of clinical pharmacologists, working at the Regional Pharmacovigilance Centre sited at University Hospital of Messina, ward physicians and monitors. The team analyzed each case of suspected ADR, to make a final causality assessment between a drug and an adverse reaction applying. Only ADR reports with a certain, probable, or possible causality assessment were included. In accordance with the Italian healthcare system, all collected ADRs were reported to the Indian Pharmacovigilance System. Additionally, for each ADR, customized information, to update the reporters about risks related to a drug's use.[21,26,28] Adverse drug reactions were codified as detailed by the Medical Dictionary for regulatory Activities (MedDRA) and organized according to the system organ class (SOC) classification and preferred term (PT). An ADRs was considered serious when it was fatal, life-threatening, required or prolonged hospitalization, caused serious or permanent disability, or congenital birth defect. The preventability of ADRs was assessed according to Shamrock and Thornton criteria. The Anatomical Therapeutic and Chemical (ATC) classification was used to code therapeutic groups (level I–IV) and active principles (level V).[25,26,28]

The diagnosis of admission and discharge at the hospital ward and concurrent diseases were coded according to the International Classification of Diseases, ninth edition, Clinical Modification (ICD-9-CM). Co morbidities were assessed by the Charlson score.

The LOS was evaluated as the number of days between the date of admission and the date of discharge or determines the rate of ADRs occurring during hospital stay, the number of inpatients who experienced an ADR divided by the total number of patients admitted to the hospital wards was considered. The prevalence of ADRs present upon admission was calculated as the ratio between the number of patients admitted for ADRs and the total number of admissions in Internal Medicine departments.[25,29,30]




❖ **Fig: - Number of ADRs Received from Different Departments.**

**ADRs FREQUENCY**

To estimate ADRs overall frequency, the total number of patients with ADRs was divided by the total number of hospital discharges during the study period and the result was multiplied by 100.[31,36]

**RESULTS**

Case-control study covering a population of National Health Service medical practitioners. All acute, non-planned admissions to all Dutch academic and general hospitals in 2021 were included in the study (n = 668 714). In 2021, hospitalizations were coded as ADR related. This was 1.93% of all acute hospital admissions in The Netherlands (96% CI 1.81, 1.85). The proportion increased with age from 0.08% (96% CI 0.76, 0.86) in the <18 years group to 3.3% in the ≥82 years group (96% CI 3.18, 3.33). The most frequent ADR-related diagnoses of hospitalizations were bleeding (n = 1049), non-specified 'unintended effect of drug' (n = 439), hypoglycemia (n = 376) and fever (n = 347). The drugs most commonly associated with ADR-related hospitalizations were anticoagulants (n = 2186), cytostatics and immunosuppressive (n = 1810) and diuretics (n = 9710). Six percent of the ADR-related hospitalizations had a fatal outcome (n = 735). Older age and female gender were associated with ADR-related hospitalizations. Only approximately 2% of the coded ADRs causing hospitalization were reported to our national centre for spontaneous ADR reporting.

**CHARACTERISTICS OF ADRs:-** A total of 159 inpatients developed 163 ADRs during their hospital stay, as some patients suffered more than one reaction. In 322 hospitalized patients for iatrogenic disease, 110 suspected adverse reactions were recorded.

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It is widely acknowledged that older patients are mainly at risk for ADRs, primarily due to increased chronic

disease, polypharmacy (concomitant prescription of five or more drugs), and age-related physiological changes affecting the pharmacokinetics and pharmacodynamics of drugs.

The potential contribution of patient reports of adverse drug reactions is discussed, both in terms of their qualitative and quantitative contribution or the diagnosis of ADRs is highly subjective and imprecise. Incidence of adverse drug reaction (ADR)-related hospitalizations has usually been assessed within hospitals. The adverse drug reaction (ADR) is an injury caused by taking medications they Define an adverse drug reaction as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, warrants prevention or specific treatment, administration and alteration of the dosage regimen. Case-control study covering a population of National Health Service medical practitioners and proportion of ADR-related hospitalizations is substantial, especially considering the fact that not all ADRs may be recognized or mentioned in discharge letters.

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## CONCLUSION

These results indicate that ADRs that occur during hospitalization or contributing to admission to Internal Medicine wards are considerable, and gender and polypharmacy are associated with their occurrence. The high incidence of preventable ADRs provides a strong rationale for undertaking future research aimed to implement interventions useful to reduce drug-related reactions and the proportion of ADR-related hospitalizations is substantial, especially considering the fact that not all ADRs may be recognized or mentioned in discharge letters. Under-reporting of ADRs that result in hospital admission to our national centre for spontaneous ADR reporting was considerable.

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