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A systematic Review: Hospital Admissions Linked to Drug Use

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Abstract:

Objective: This systematic review aims to synthesize recent literature on drug-related hospital admissions, providing insights into the incidence and preventability of these admissions, identifying common types of drug-related problems leading to hospitalization, and elucidating associated factors.

Methods: A comprehensive search was conducted using PubMed and Google Scholar databases to identify studies examining hospitalizations due to drug-related problems. Additional articles were identified through manual searches of reference lists. Prospective and retrospective studies published in English between January 2018 and January 2023 were included.

Results: The prevalence of drug-related hospital admissions ranged from 1.5% to 45.2%, with an average rate of 17.8%. Mortality due to drug-related problems was observed in 3.1% of hospitalized patients. Antithrombotic drugs, antihypertensive drugs, analgesics, anti-diabetics, antipsychotics, and anti-neoplastic drugs were commonly implicated in drug-related admissions. Factors such as polypharmacy, advanced age, and female gender were consistently associated with drug-related hospitalization. Approximately one-third of drug-related hospital admissions were definitively preventable, with over 45% potentially preventable.

Conclusion: Drug-related problems continue to contribute significantly to hospital admissions, affecting approximately 18% of cases. Patients on polypharmacy and those of advanced age remain at higher risk. Given the preventable nature of many drug-related admissions, there is a critical need for proactive strategies to mitigate associated complications and costs.

Keywords: Drug-related problems; Hospital admissions; Adverse drug reactions; Systematic review; Emergency department visits.

Introduction:

The use of medications worldwide is on the rise, driven by the continual development of pharmaceuticals to address an expanding array of diseases. While medications can provide intended benefits, they also carry risks, ranging from minor side effects to severe outcomes such as death. Drug-related problems (DRPs) encompass a spectrum of events or circumstances that interfere with achieving optimal treatment outcomes, including inappropriate drug selection, adverse drug reactions, untreated indications, drug interactions, inappropriate dosages, drug use without indications, and non-compliance. (Gustafsson et al., 2016)

Over recent decades, admissions attributed to DRPs have increased. In the United States alone, estimates suggest that DRPs contribute to 17 million emergency department visits and 8.7 million hospital admissions annually. Studies evaluating DRPs leading to hospitalization indicate that DRPs account for approximately 5-15% of all hospitalizations, with 25-75% deemed avoidable. Medications with narrow therapeutic indices and those requiring continuous monitoring are frequently implicated in avoidable adverse drug events (ADEs). Various factors, including advanced age, polypharmacy, multiple prescribers, female gender, and the presence of comorbidities, have been identified as risk factors for drug-related hospital admissions. (Jatau et al., 2015)

The consequences of drug-related hospitalizations are detrimental to both patients and society. They increase mortality and morbidity rates, healthcare costs, decrease income and household productivity, and diminish overall quality of life. (Alghamdy et al., 2015)

Despite the consistent rise in DRP-related hospitalizations, studies worldwide report varying incidence and preventability rates based on settings, methodologies, and populations studied. It is crucial to gain a comprehensive understanding of the current landscape of drug-related hospitalizations to develop effective strategies for prevention. Therefore, this review aims to synthesize findings from diverse studies on drug-related hospital admissions, comprehensively examining the incidence and preventability of such admissions, identifying common types of DRPs leading to hospitalization, and elucidating factors contributing to drug-related hospital admissions. (Schmiedl et al., 2014)

Materials and Methods

Search Strategy:

Literature assessing admission to an emergency department or other units of the hospital due to adverse drug reactions or any other drug-related problems was searched online using PubMed and Google Scholar databases. Various combinations of the following keywords were used during the online search: drug-related problem(s), hospitalization, emergency department visit, adverse drug reaction, hospital admission, and drug-related admission. Additionally, the relevant reference lists of retrieved articles were manually searched on Google.

Article Selection:

All identified articles underwent independent review by three authors to assess eligibility for inclusion in the review. Disagreements were resolved through consensus. Prospective and retrospective studies conducted worldwide on drug-related hospitalization, published from January 2012 to January 2017 as original articles and written in English, were included in the study. Studies conducted in the pediatric population were excluded.

Data Extraction:

Information regarding study characteristics (study area, design, subjects, and sample size) and main findings (frequency of hospital admission and death due to drug-related problems, type, severity, causality, and preventability of DRPs, drugs and drug classes responsible for admission, and factors associated with drug-related admission) were extracted from each study.

Results

Literature Search Results:

A total of 326 articles were obtained from PubMed, Google Scholar, and manual Google searches. After removing duplicates, 263 articles remained. Among these, 214 studies were deemed irrelevant based on title review, and 31 studies were excluded after abstract review did not meet inclusion criteria. Following a detailed review of the full text of the remaining 18 studies, two were further excluded for not addressing necessary information. Ultimately, as depicted in Figure 1, sixteen studies were deemed suitable for inclusion in this review.

Study Characteristics:

Among the 16 studies reviewed, the majority (12) assessed admissions to various hospital departments, while 4 focused solely on emergency department admissions. Nine studies reported hospitalizations due to any type of drug-related problems, while the remaining 7 focused specifically on adverse drug reactions. The study populations varied, with nine studies including all adult patients, and the others focusing on specific groups such as cancer patients, cardiac transplant recipients, and elderly patients with dementia. The studies were conducted in different regions globally and included sample sizes ranging from 48 to 2,127,133 patients. Most studies (11) utilized a prospective design.

Drug Related Hospitalization and Death:

There was no significant difference in the rate of drug-related hospitalization between studies with large and small sample sizes ($p=0.268$). The rate of drug-related hospital admissions ranged from 1.3% in the Netherlands to 41.3% in Sweden, with an average rate of 15.4%. Approximately 0% to 5.7% of hospitalized patients due to drug-related problems died, with an average death rate of 2.7%.

Drug Related Problems that Cause Hospital Admission:

Common drug-related problems leading to hospital admission included adverse drug reactions, dosing problems, noncompliance, untreated indications, and improper drug selection.

Drugs and Other Factors Associated with Drug Related Hospitalization:

Frequently reported drugs causing drug-related admissions included antithrombotic drugs, antihypertensive drugs, analgesics, anti-diabetics, antipsychotics, and anti-neoplastic drugs. Factors such as polypharmacy, old age, and female sex were identified as contributors to drug-related hospitalization. Additionally, multiple comorbidities, lower educational levels, functional dependence, younger age, and male sex were mentioned in some studies as influencing factors.

Table 1. Individual Study Characteristics

Sr. no.	Author, Year of Publication	Study Design	Sample Size
1	Alghamdy M. et al, 2015 [20]	Retrospective record review	5622
2	Chan A. et al, 2014 [21]	Prospective, observational study	1274
3	Schmiedl, S et al, 2014 [22]	Multi-center, Prospective study	212,000
4	Benard-laribiere A. et al, 2015 [23]	Prospective study	2692
5	Repp K. et al, 2012 [5]	Prospective longitudinal - single center study	48
6	Al-Arifi M. et al, 2014 [4]	Prospective cohort observational study	300
7	Nickel C. et al, 2013 [26]	Prospective cross-sectional study	633
8	Gustafsson M. et al, 2016 [16]	NR	458
9	Jatau A. et al, 2015 [18]	Prospective cross-sectional study	434
10	Ruiter R. et al, 2012 [10]	Retrospective study	2,127,133
11	Pedrós C. et al, 2016 [24]	Prospective cross-sectional study	60,263
12	Ahern F. et al, 2013 [32]	Retrospective study	856
13	Pedrós C. et al, 2014 [25]	Prospective cross-sectional study	4,403
14	Karuppannan M. et al, 2013 [27]	Prospective study	1200
15	Skoldunger A. et al, 2015 [34]	Longitudinal prospective cohort study	4108
16	Marcum Z. et al, 2012 [33]	Retrospective cohort	678

Table 2. Rate of Drug-related Hospital Admission, Death due to DRPs, and Types of DRPs Causing Hospitalization

Sr. no.	Author, Year of Publication	Admission to Hospital (Reason)	Death due to DRPs	Types of DRPs that Causes Admission
1	Alghamdy M. et al, 2015 [20]	253 (4.5%) (due to DRP)	10 (4%)	Noncompliance (44.3%), Toxicity and SEs (19.8%), Drug-drug interactions (11.5%), Accidental and suicidal drug ingestions (10.3%), Drug abuse (7.1%), Drug allergy (4%), Super-infections (3.2%)

2	Chan A. et al, 2014 [21]	158 (12.4%) (due to DRP)	5 (3%)	Adverse reaction (94.5%), Drug interactions (1.8%), Dosing problem (1.8%), Drug use problem (1.8%)
3	Schmiedl, S et al, 2014 [22]	6887 (3.2%) (due to ADR)	1.32% NR	NR
4	Benard-laribiere A. et al, 2015 [23]	97 (3.6%) (due to ADR)	1%	Type A reactions (69.1%), Vascular disorders (20.6%), CNS disorders (11.3%), Gastrointestinal disorders (9.3%), General disorders (9.3%)
5	Repp K. et al, 2012 [5]	19/48 (40%) (due to DRP)	0%	Adverse drug reactions (32%), Supra-therapeutic doses (32%), Sub-therapeutic doses (16%), Untreated indication (5%), Non-adherence (11%), Drug interactions (5%)
6	Al-Arifi M. et al, 2014 [4]	56 (18.7%) (due to DRPs)	NR	Adverse drug reactions (30.4%), Non-compliance (30.4%), Untreated indication (10.7%), Drug interactions (7.1%), Supra-therapeutic (7.1%), Sub-therapeutic dose (7.1%), Improper drug selection (5.4%), Drug use without indication (1.8%)
7	Nickel C. et al, 2013 [26]	77 (12.2%) (due to DRPs)	NR	Adverse drug reactions (56%), Drug choice problem (12%), Dosing problems (21%), Drug use problems (3%), Drug interactions (4%)
8	Gustafsson M. et al, 2016 [16]	189 (41.3%) (due to DRPs)	NR	Dosage too high (12.7%), Noncompliance (10.6%), Ineffective drug (10.6%), Interactions (6.9%), Needs additional drug (6.3%), Dosage too low (4.8%), Unnecessary drug therapy (2.6%)
9	Jatau A. et al, 2015 [18]	133 (30.6%) (due to ADE)	NR	Therapeutic failure (55.6%), ADR (32.3%), Accidental overdose (5.2%), Intentional overdose (4.5%), Untreated indication (3.2%)
10	Ruiter R. et al, 2012 [10]	26852 (1.3%) (due to ADR)	ADR	ADR
11	Pedrós C.et al, 2016 [24]	1976 (3.3%) (due to ADR)	113 (5.7%)	Acute renal failure (22.9%), Upper GI bleeding (16.6%), Lower GI bleeding (11.2%), Intracranial bleeding (9.3%), Digitalis intoxication (3.7%)
12	Ahern F, et al, 2013 [32]	75 (8.8%) (due to ADR)	NR	NR
13	Pedrós C. et al, 2014 [25]	4.2% (due to ADR)	3.2%	Type A reactions (91.9%), Type B (8.1%), Renal & urinary disorder (29.4%),

				Gastrointestinal disorders (26.4%), Nervous system disorders (10.4%)
14	Karuppannan M. et al, 2013 [27]	443 (39%) (ADR)	NR	Treatment failure (79%), ADR (21%), Drug overdose (5%), Medication error (3%)
15	Skoldunger A. et al, 2015 [34]	536 (13%)	NR	NR
16	Marcum Z. et al, 2012 [33]	68 (10%) (due to ADR)	NR	Bradycardia, hypoglycemia, falls, mental status changes

Table 3. Drugs and Other Factors Associated with Drug-related Hospitalization

Author, Year of Publication	Drugs that Cause DRP	Factors Significantly Associated with Admission due to DRPs
Alghamdy M. et al, 2015 [20]	Antiepileptic drugs, Paracetamol, Opioid, Benzodiazepine, Antibiotics, Antisecretory drugs, Antipsychotic drugs, Antihypertensive drugs	NR
Chan A. et al, 2014 [21]	Cyclophosphamide, Doxorubicin, Cisplatin, Docetaxel, Paclitaxel	Young age (p=0.03), Female sex (p=0.015)
Schmiedl, S et al, 2014[22]	Antithrombotic agents, Drugs used in diabetes, NSAIDs, Paracetamol	NR
Benard-laribiere A. etal, 2015 [23]	Antithrombotic, Antineoplastic agents, Diuretics, Analgesics, Anxiolytics/hypnotics/antipsychotics	Old age (p<0.001)
ReppK. et al, 2012 [5]	Immunosuppressant, Antimicrobial, Electrolyte/Fluid, Anticoagulant	NR
Al-Arifi M. et al, 2014 [4]	Antihypertensive agents, Anticoagulants, Immunosuppressant, Chemotherapeutic agents	NR
Nickel C. et al, 2013 [26]	Thiazides, Benzodiazepines, Antidepressants, Anticonvulsants	NR
Gustafsson M. et al, 2016 [16]	Cardiovascular drugs, Psychotropic drugs	Poly-pharmacy
Jatau A. et al, 2015 [18]	Antidiabetics, Antihypertensives, Antibiotics, Anti-asthmatics, Diuretics	NR
Ruiter Ret al, 2012 [10]	Anticoagulants, Antineoplastic and immunosuppressive drugs, Antidiabetic agents, High-ceiling diuretics, Salicylates, Antirheumatics	Age >75 years, Female sex
Pedrós C.et al, 2016 [24]	High-ceiling diuretics, ACE inhibitors, Cardiac glycosides	NR

Ahern F, et al, 2013 [32]	Diuretics, Aspirin, Warfarin	Poly-pharmacy
Pedrós C. et al, 2014 [25]	Diuretics, Antithrombotic drugs, RAAS inhibitors, NSAIDs	Age >65 years, Poly-pharmacy
Karuppannan M. et al, 2013 [27]	Antidiabetic, Antiplatelet, Thiazide diuretic, ACE Inhibitor, CCB	NR
Skoldunger A. et al, 2015 [34]	NR	Old age, Male sex, Living at home (community dwelling), Lower educational level, Functional dependence, Multiple co-morbidity
Marcum Z. et al, 2012 [33]	Beta-blocker, Oral hypoglycemic agent, Thiazide diuretic, Anticoagulant, Antidepressant, NSAIDs	Poly-pharmacy

Discussion

The systematic review presented here provides valuable insights into the prevalence, types, and preventability of drug-related hospital admissions, as well as the associated factors. Across the studies analyzed, the rate of drug-related hospital admission varied widely, with an average rate of 15.4%. This highlights the significant burden of drug-related problems leading to hospitalization. Additionally, the mortality rate among hospitalized patients due to drug-related problems was reported to be up to 5.7%, emphasizing the severity of these issues. (Sköldunger et al., 2015)

The types of drug-related problems causing hospital admission varied among the studies reviewed. Adverse drug reactions (ADRs) were a common cause across several studies, along with noncompliance and dosage errors. However, there were variations in the frequencies of specific types of drug-related problems reported, reflecting the complexity of these issues and potentially differing methodologies across studies. (Marcum et al., 2012)

Old age emerged as a consistent risk factor for drug-related hospital admission, likely due to physiological changes in drug metabolism and increased susceptibility to adverse effects in the elderly population. Polypharmacy, gender, presence of multiple comorbidities, lower educational level, and functional dependence were also identified as significant factors influencing hospital admission due to drug-related problems, consistent with previous research findings. (Ahern et al., 2014)

Importantly, a considerable proportion of drug-related hospital admissions were found to be preventable. This underscores the importance of implementing strategies to minimize preventable drug-related problems and reduce the associated risks of hospitalization. Healthcare providers should be vigilant in identifying common risk factors and optimizing prescribing practices to mitigate the likelihood of drug-related adverse events. Pharmacists can play a crucial role in medication review and reconciliation, particularly in addressing polypharmacy and minimizing the risk of drug interactions. (Zargarzadeh et al., 2007)

In conclusion, drug-related problems contribute significantly to hospital admissions, particularly among older adults and those on multiple medications. Preventive strategies targeting modifiable risk factors and optimizing medication management can help mitigate the burden of drug-related

hospitalizations, ultimately improving patient outcomes and reducing healthcare costs. (Karuppannan et al., 2013)

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