A study on medication-related hospital admissions in a tertiary care hospital

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**Abstract:**
Medication-related hospital admissions have gained attention during the last few decades. It has been reported that up to 5% of all hospital admissions were medication-related and 50% of those were avoidable. In India, studies on medication-related hospital admissions are still in the infancy stage. The objective of the study was to assess the types and outcomes of medication-related hospital admissions (MRHA) in a tertiary care teaching hospital. This prospective observational study was conducted for six months at JSS Hospital, Mysuru. Patients of any age and gender, who were admitted to General Medicine, Emergency, Nephrology, Psychiatry, Pulmonology wards due to medication-related problems were enrolled in the study after obtaining an Inform Consent Form. All the necessary data about MRPs were collected and documented in a suitably designed data collection form. MRPs were classified by using Hepler and Strand classification, and the implicated drugs were coded by using the Anatomical Therapeutic Chemical Classification system (ATC) code. Prevalence of medication-related admissions was calculated by dividing the total number of medication-related admissions and the total number of admissions to the hospital. There were 185 MRHA during the study period in the respective departments. The total prevalence of MRHA in the included departments was 1.27%. Failure to receive drugs (50.27%) accounted for the maximum MRHA, followed by adverse drug reactions (46.44%) and overdose (3.27%). The average cost associated with MRHA was found as INR 10,440 (USD-174, £-149). The average length of stay of MRHA was found as approximately seven days [6.96, (sd ±2.42)]. The study shows that failure to receive drugs leading to hospitalization are frequent and constitute a significant economic burden. Training of patients and prescribers may lead to a reduction in hospitalization due to MRPs and thus lessen their financial burden.

**Introduction**

The 2018 World Drug Report (WDR) by the United Nations Office on Drugs and Crime (UNODC) states that medication use has increased in recent years. Advances in the pharmaceutical industry have introduced a vast number of agents to manage the broad spectrum of diseases that increased demands for intensifying therapeutic challenges. Most commonly, the people benefit from pharmacotherapeutic interventions; however, adverse events ranging
A Drug-related problem (DRP) is defined as an event or circumstance that involves a patient’s drug treatment that actually, or potentially, interferes with the achievement of an optimal outcome (Easton et al., 2004; Hepler and Strand, 1990). The proportion of elderly emergency admissions that were drug-related hospital admissions (DRHA) varied between 15% and 22% in Australian studies (Chan et al., 2001). In Australia, the incidence rate of DRHA was found between 2.4% and 3.6% and in the United States, between 3.1% and 6.2%. In India, DRHA was found to be 0.20%. Although many DRPs can be resolved without a significant impact on a patient’s health, some of them can be associated with considerable morbidity and mortality. If left untreated, drug-related morbidity may ultimately lead to drug-related mortality (Sekhar et al., 2011). Many of the outpatient medications resulting in hospital department visits and admissions were found to be underreported in existing administrative data capturing system in the hospitals (Hohl et al., 2013).

The cost associated with drug-related hospital admissions is yet another field which has to be explored. Therefore, it is necessary to undertake a study on drug-related Hospital admissions; to assess the prevalence of drug-related hospital admissions, to identify and classify the drug-related problems leading to hospital admission, to estimate the cost associated with the drug-related hospital admissions and to determine the predictors of drug-related issues in the study population. Besides, most of the researches evaluating drug-related visits to the emergency department has involved retrospective studies or analysis of administrative data. Retrospective studies may underestimate the incidence of drug-related visits because information may be missing or inaccurately documented. In such a situation, a prospective survey of drug-related hospital admissions can come up with a large pool of efficient data, which can be effectively utilized to estimate the underlying cause behind drug-related hospital admissions and to analyze the cost associated with the drug-related hospital admissions.

**METHODOLOGY**

This was a prospective observational study conducted for six months in in-patient wards (Medicine, Emergency, Nephrology, Pulmonology, and Psychiatry) of 1,800-bed tertiary care teaching hospital with different specialities providing health care facilities to the people residing in and around the district of Mysuru. The Institutional Ethics Committee approved this study of the college. Patients of either gender of all ages admitted to General Medicine, Emergency, Nephrology, Pulmonology and Psychiatry wards of the hospital due to medication-related problems were included in the study, reviewed and followed daily till discharge. Hospital admissions due to poisoning by chemical entities other than drugs were excluded from the study. All the required data were collected, and the same was documented in a suitably designed data collection form. The medication-related problems (MRPs) identified were categorized using Hepler and Strand classification. After identifying MRPs, an attempt was made to identify the origin or root of the problem. The various causes for the issues like lack of knowledge of health care professional’s (HCPs), prescribing practice, the workload of HCPs, lack of time to monitor the patients, poor compliance of patients due to unawareness, high cost of drugs and any other patient-related issues were documented.

The prevalence of MRPs was calculated by taking the ratio of the number of patients who experienced MRPs to the total number of admissions to the hospital. The MRPs in each Hepler & Strand class are reported in numbers and percentages. Means and standard deviations for cost assessment was performed in MS Excel. Using the chi-square test, predictors associated with the MRPs were identified with a p-value of <0.05. The variables tested for identification of predictors included age and gender. The statistical analysis was performed by using Statistical software (IBM-SPSS) version 20.0. A p-value <0.05 was considered as statistically significant.

The total cost associated with MRHA included medication charges, laboratory charges, bed charges, consultation fees and miscellaneous charges. This cost analysis excluded food charge and discharge mediation cost. The costs calculated were converted to dollars by assuming 1 dollar = 76 Indian rupees and Euro by taking 1 Euro = 82 rupees.

**RESULTS AND DISCUSSION**

Patients admitted to emergency, medicine, pulmonology, nephrology and psychiatry who met the inclusion criteria were included in the study. Prevalence of MRHA was calculated from this data as 1.27%. It can be observed from the data that the prevalence of MRHA is most in medicine department (3.6%). Prevalence from different departments is shown in Table 1.

While most of the studies restrict drug-related hospital visits and admissions to the emergency department, MRHA in five significant departments were analyzed in this study. A meta-analysis with 95 stud-
Table 1: Prevalence per cent of MRHA in individual departments

| Department      | MRHA N | Total admissions N | Prevalence % |
|-----------------|--------|--------------------|--------------|
| Emergency       | 38     | 9825               | 0.39         |
| Medicine        | 130    | 3621               | 3.6          |
| Pulmonology     | 4      | 381                | 1.04         |
| Nephrology      | 9      | 379                | 2.37         |
| Psychiatry      | 2      | 189                | 1.1          |

Table 2: Demographics details of the participants

| Department      | Total MRHA | Parameters        |
|-----------------|------------|-------------------|
|                 | Gender n (%) | Age n (%)         |
|                 | Male | Female | <20 | 21-40 | 41-60 | >61 |
| Emergency       | 38   | 18 (47.36) | 20 (52.63) | 4 (10.52) | 11 (28.84) | 10 (26.31) | 13 (34.21) |
| Medicine        | 130  | 66 (50.76) | 64 (49.23) | 3 (2.30) | 15 (11.53) | 54 (41.53) | 58 (44.64) |
| Pulmonology     | 4    | 2 (50) | 2 (50) | 0 | 1 (25) | 3 (75) | 0 |
| Nephrology      | 9    | 6 (66.66) | 3 (33.33) | 0 | 2 (22.22) | 2 (22.22) | 5 (55.55) |
| Psychiatry      | 2    | 2 (100) | 0 | 1 | 1 (50) | 0 | 0 |
| Total           | 183  | 94 (51.36) | 89 (48.63) | 8 | 30 (4.37) | 69 (37.70) | 76 (41.53) |

Table 3: Types of MRPs observed in the study population

| MRP                | Total DRPs n (%) | EMD n (%) | Med n (%) | Pulmon n (%) | Nephro n (%) | Psychiatry n (%) |
|--------------------|-----------------|-----------|-----------|--------------|--------------|-----------------|
| Failure to receive drug | 92 (50.27) | 8 (8.69) | 80 (86.95) | 1 (1.08) | 2 (2.17) | 1 (1.08) |
| Overdose           | 6 (3.27) | 6 (100) | 0 | 0 | 0 | 0 |
| ADRs               | 85 (46.44) | 24 (28.23) | 50 (58.82) | 3 (3.52) | 7 (8.23) | 1 (1.17) |

ies reported a range of prevalence of medication-related hospitalization between 0.1 to 54% (Leendertse et al., 2008). These variances in reported prevalence are as a result of the study setting, studied population, method of data collection and the continent in which the study is performed.

Among the patients enrolled in the study, 94 patients (51.3%) were male and 89 patients (48.6%) as female making up a male: female ratio of 1.1:1. The patients enrolled in the study were further classified based on the age group. The number of patients with age less than 20 was 8(4.37%), 21-40 were 30(16.39%), between 41-60 were 69(37.70%) and age greater than 61 were 76(41.53%). Demographic data of the study population are as shown in Table 2.

Types of medication-related problems (MRP)

The identified MRPs resulting in hospital admissions were classified as per Hepler and stands classification. Failure to receive drugs (50.27%)
### Table 4: ATC classification of drugs which resulted in hospital admissions

| ATC code | ATC class                              | Total DRPs n (%) | Hepler and Strands classification of DRP n (%) |
|----------|----------------------------------------|------------------|-----------------------------------------------|
|          |                                        |                  | Failure to receive drugs                       | ADRs | Overdose |
| A        | Alimentary tract and metabolism        | 72 (39.34)       | 48 (66.66)                                    | 24 (33.33) | 0 |
| C        | Cardiovascular system                  | 39 (21.31)       | 26 (66.66)                                    | 13 (33.33) | 0 |
| H        | Systemic hormonal preparations         | 3 (1.63)         | 3 (100)                                       | 0 | 0 |
| J        | General Anti-infective system          | 12 (6.55)        | 1 (8.33)                                      | 11 (91.66) | 0 |
| L        | Antineoplastic and Immunomodulating agents | 5 (2.73)     | 0                                             | 5 (100) | 0 |
| M        | Musculoskeletal system system          | 8 (4.37)         | 0                                             | 8 (100) | 0 |
|          | Nervous system                         | 32 (17.48)       | 9 (28.12)                                     | 17 (53.12) | 6 |
| R        | Respiratory system                     | 11 (6.01)        | 8 (72.72)                                     | 3 (27.27) | 0 |
| S        | Sensory organs                         | 1 (0.54)         | 0                                             | 1 (100) | 0 |

### Table 5: Age and failure to receive drug-related hospital admissions

| Age   | No. of inability to receive drugs n (%) | Male n (%) | Female n (%) |
|-------|----------------------------------------|------------|--------------|
| <20   | 3 (3.26)                               | 3 (100)    | 0            |
| 21-40 | 11 (11.95)                             | 7 (63.63)  | 4 (36.36)    |
| 41-60 | 35 (28.04)                             | 21 (60)    | 14 (40)      |
| >61   | 43 (46.73)                             | 25 (58.14) | 18 (41.86)   |

### Table 6: Cost associated with drug-related hospital admissions

| DRP                | Average Cost | Sd (INR) |
|--------------------|--------------|----------|
|                    | INR          | USD      | Euro     | ±             |
| ADRs               | 8571         | 143      | 122      | 4873.03       |
| Failure to receive drugs | 12271       | 205      | 175      | 8445.19       |
| Overdose           | 8853         | 148      | 126      | 3380.51       |
Table 7: Length of stay for drug-related hospital admissions

| DRP                     | Avg length of stay | Sd    |
|-------------------------|--------------------|-------|
| ADRs                    | Seven days         | ±2.17 days |
| Failure to receive drugs| Seven days         | ±2.56 days |
| Overdose                | Six days           | ±2.94 days |

Figure 1: Drugs most associated with hospital admissions

Figure 2: Gender and failure to receive drugs-related hospital admission

Figure 3: Department wise classification of failure to receive drugs-related hospital admission

Figure 4: Reason for failure to receive drug-related hospital admission

accounted for the maximum MRHA, followed by ADRs (46.44%) and overdose (3.27%). Among the failure to receive drugs, maximum cases were admitted in the medicine ward (86.95%). ADRs were the second major cause of MRHA which resulted in hospital admission in 46.44%. Maximum ADR related hospitalization was seen in medicine ward (58.82%) followed by emergency (28.23%), Pulmonology (3.52%), Nephrology (8.23%) and psychiatry (1.17%). There were six overdoses related hospitalization (3.27%), all of which were admitted to the emergency department. Types of MRPs observed in the study population is as shown in Table 3.

These distributions of MRHA were similar to the study by Harminder Singh et al., conducted in a north Indian hospital. They had identified non-compliance (46.6%) as the chief problem, which resulted in hospitalization, followed by ADRs (22.03%) (Singh et al., 2011). But in many European and American studies, ADRs dominate as the reason for admissions than failure to receive drugs. A Canadian survey of Peter J Zed et al. had shown ADR as the prime reason for admission (39.3%), followed by non-adherence (27.9%) (Zed et al., 2013).

Drugs implicated

ATC classifications were used to classify all the drugs which resulted in hospital admissions. Drugs classified under ATC code A (Alimentary tract and metabolism) were most associated with hospital admissions (39.34 %), and the main reason for hospital admissions with ATC code A was found to be a failure to receive drugs (66.66%) which is followed by ADRs (33.33%). Drugs classified under ATC code C (Cardiovascular system) ranked second in the hospital admissions (21.31%). Thirty-two hospital admissions (17.48%) were found to be caused by nervous system drugs [ADR= 53.12%, failure to receive drugs 28.12%, overdose 18.75]. General anti-infective system drugs accounted for 6.55% of which 91.66 % were due to ADR, and 8.33% were
due to failure to receive medicines. Medicines that were responsible for MHRA along with their respective ATC codes are shown in Table 4.

Respiratory resulted in 6.01% (11 cases) of the hospital admissions [failure to receive drugs -72.72% (8 cases), ADRs -27.27% (3 cases). There were eight hospital admissions (4.37%) which were due to drugs belong to the class musculoskeletal system [ADR-8 cases (100%)]2.73% of drugs which caused hospital admissions were belonging to the class antineoplastic and Immunomodulating agents (ADR-5 cases), 1.63% of drugs belonging to systemic hormonal preparations (failure to receive drugs -3 cases) and 0.54% of drugs belonging to the class sensory organs (failure to receive drugs -1 case).

We can see a wide variation in drugs, causing hospital admissions from continent to continent. Mohamed Al Arifi et al. studied about MRHA in Riyadh military hospital showed that Anti-hypertensive medications (16.1%) were the major cause for MRHA followed by Anticoagulants (14.3%), Immunosuppressant’s (12.5%), Chemotherapy drugs (10.7%), Antipsychotics (7.1%), Insulin’s (3.6%), Anticonvulsants (3.6%) followed by other class of drugs (Mohamed Al Arifi et al., 2013).

A study on MRHA in a tertiary care hospital in south India has shown that central nervous system drugs are the major contributors for MRHA (203 cases,35.5%), followed by Cardiovascular drugs (114 cases,19.8%), NSAIDs (71 cases,12.3%), Antibiotics (65 cases,11.3%), Anticoagulant (57 cases,9.9%), followed by other drugs (65 cases,11.3%) (Sekhar et al., 2011). These variations in medicines which resulted in hospital admissions may be due to prescription pattern, disease pattern, method of drug dispensing, study setting, study population and nature of data collection.

Drugs most associated with hospital admissions.

The drug most associated with MRHA was identified as Tab. Glimperide+Metformin 1+500 mg given per oral for type II Diabetes mellitus. It was observed that the drug omission by the patient (36 cases, 83.72%) accounted for a maximum of Tab. Glimperide+ Metformin related to hospital admissions. 16.27% (7 cases) of Tab. Glimperide+ Metformin related admissions were due to ADR. Insulin resulted in 18 MRHA, of which 55.55% (10 cases) of the admissions were due to ADRs, and 44.44% (8 cases) of the admissions were due to failure to receive drugs. Tab. Amlodipine, the most frequently used anti-hypertensive resulted in 15 hospital admissions of which 86.66% (13 cases) were due to failure to receive drugs, and 13.33% (2 cases) of cases were due to ADRs. Tab. Diclofenac which is yet another NSAID caused 11 hospital admissions, of which 4 cases (36.36%) were caused due to ADRs, 5 cases (45.45%) were caused due to failure to receive drugs and 2 cases (18.18%) were caused by drug overdose. Tab. Ibuprofen which is a most common NSAID used in hospital resulted in 1 hospital admission, of which all were due to ADRs. Tab. Phenytoin caused 11 hospital admissions of which 4 cases (36.36%) were caused due to ADRs, 5 cases (45.45%) were caused due to failure to receive drugs and 2 cases (18.18%) were caused by drug overdose. Tab. Diclofenac which is the most common NSAID used in hospital resulted in 9 hospital admissions of which all were caused due to ADRs. Tab. Ibuprofen which is yet another NSAID resulted in 5 hospital admissions, of which all were attributed to be a result of ADRs. These results cannot not be compared with other studies because of the variances with study setting and studied population. Drugs most associated with hospital admissions is depicted in Figure 1.

Failure to receive drug-related hospital admission.

Drug-related hospital admissions due to failure to receive drugs were most common in medicine department (86.95%, 80 cases), followed by emergency (8.69%, 8 cases), nephrology (2.17% 2 cases) and psychiatry and pulmonology (1.08%, 1 case each). 56 (60.86%) males and 36 (39.13%) females were admitted due to failure to receive drug making a male: female ratio of 1.55:1. In medicine department, out of 80 admissions, 47 (58.75%) were males, and 33 cases (41.25%) were females. These data points out that males are more related to omission and underutilization of medication resulting in hospital admissions than females. But in the nephrology department, male: female ratio was 1:1(1 case each) which shows males and females are equally associated with failure to receive drug-related hospitalization Figure 2. Data about the department wise classification of inability to receive drugs-related hospital admissions is depicted in Figure 3.

It can be seen that age > 61 is a risk factor for failure to receive drug-related hospital admissions. Among the 92 failure to receive related hospital admissions, 46.73% (43 cases) were belonging to the age group above 61 Table 5. Statistical analysis with by chi-square test (IBM SPSS statistics 10) has shown that this data is statistically significant (p-value 000). In the age group >61, the male: female ratio was calculated as 1.38:1, adding up that male geriatric patients are more associated with failure to drug-related hospitalization. It can be seen that found chances of drug-related hospital admissions due to failure to receive drugs increases with age. [age ≤20 – 3.26% (3 cases), age 21-40 -11.95% (11 cases)
age 41-60 28.04 % (35 cases), age >61 46.73 % (43 cases]). The major reason for more geriatric failure to receive drug-related hospital admissions may be unawareness, forgettability, attitude, ADRs and economic burden caused by the drugs as depicted in Figure 4. In the age group 21-40 out of the 11 drug-related hospital admissions due to failure to receive drugs (11.95%), seven admissions were male (63.63%), and four admissions were female (36.36%). Age group less than 20 reported only 3 (2.35%) drug-related hospital admissions due to failure to receive drugs, out of which all the admissions were male patients (3 cases).

Unawareness can be identified as the main reason for drug-related hospital admissions due to failure to receive medicines. 40.21% (37 admissions) of the admissions were due to unawareness of the patients regarding the need for medication adherence. This unawareness related hospital admissions would have been prevented if a clinical pharmacist initiated patient counselling was conducted while prescribing and dispensing the drugs. A clinical pharmacist can play a significant role along with other health care providers to ensure safe and productive use of medications. 25 % (23 cases) of the admissions were because of forgettability of the patient. Age could have been a risk factor which added up to the forgettability to take drugs. A clinical pharmacist initiated patient counselling to the patient caretakers would have reduced the forgettability related patient admissions. The attitude was identified as the reason for non-adherence to medication, which resulted in 17.39% (16 cases) of the admissions. 10.86 % (10 cases) of the patients were non-adherent to the medication because of the economic burden caused by medications. Lack of centralized insurance system, which includes insurance coverage to all the common people of India could have reduced this financial burden caused by drugs. We could not identify any patient who was non-adherent to medication because of ADRs.

Cost Associated with Drug-related hospital admissions.

The total cost associated with 183 hospital admissions were calculated as INR 19, 10,583 (USD-31843, £-27294). The average cost associated with MRHA was found as INR 10,440 [USD-174, £-149 (Sd ± 7024.198)] ADR related hospital admissions imposed INR 8571 [USD-143, £-122 (Sd±4873.03)] on the patients. Failure to receive drugs resulted in a hospital charge of INR 12271 [USD-205, £-175 (Sd±8445.19)]. Overdose of drugs resulting in hospital admissions was associated with a cost of INR 8553 [USD-148, £-126 (Sd±3380.51)]. While most of the MRHA studies restrict themselves to the calculation of prevalence and classification of DRPs, our research has an advantage of cost analysis with drug-related admissions. The cost associated with drug-related hospital admissions in the study is, as shown in Table 6.

K J Patel et al. in 2003 has identified the cost of ADR related hospital admission as INR 6197 (USD-150) which is comparatively low compared to the present study (INR- 8521) (Patel et al., 2007). This variation in cost shows that the health care cost of ADR related hospital admissions has gone up by approximately INR 2000 in last 12 years.

Length of Stay

The average length of stay of DRHA was found as approximately seven days [6.96, (sd±2.42)]. ADRs as a reason for admission resulted in a length of stay of 7 days about [6.63, (sd±2.17)]. Failure to receive drugs resulted in approximately seven days [7.28, (sd±2.56)] stay in hospital. Overdose as a reason for admission showed comparatively a day’s less stay (6 days) in hospital [6.33, (sd±2.94)]. Jennie et al. study on drug-related emergency department visits showed an average length of stay of 9.3 days for the elderly population (Yee et al., 2005). These variations in the length of stay may be because of differences in the study population, hospital policies and availability of central insurance schemes in developed countries which reduces the economic burden on the patients thereby making the patient stay in the hospital until complete recovery. Length of stay for drug-related hospital admissions during the study is shown in Table 7.

Predictors associated with DRHA

Age >61 for drug-related hospital admissions due to failure to receive drugs

Age >61 was most associated with failure to receive drug-related hospital admissions. [Age > 61 [46.73 % (43 cases)]. Statistical analysis with chi-square test (IBM SPSS statistics 10) has shown that this data is statistically significant (p-value 000).

Female gender for ADR related hospital admissions

Thirty-seven males (43.52%) and 48 females (56.47%) were admitted due to ADRs with a male: female ratio of 1:1.29. This data, when analyzed by the chi-square test (IBM SPSS statistics 10), was found highly significant. This data supports the fact that females are more prone to develop ADRs than males.

Multiple disease state and polypharmacy

Previous studies done by Singh et al. have identified...
multiple disease states and polypharmacy as predictors for DRHA (Singh et al., 2011). But in our study, we couldn't generate accurate data on the same because of the lack of medical records and medical knowledge with the patient.

CONCLUSION

There were 183 MRHA during the study period in the study departments. The total prevalence of DRHA in this department was 1.27%. Medicine department showed the maximum prevalence with a prevalence percentage of 3.6%, followed by nephrology 2.37% psychiatry 1.1%, pulmonology 1.04% and emergency 0.39%. The average length of stay of DRHA was found as approximately seven days [6.96, (sd±2.42)]. The MRHA were classified based on Hepler and Strands classification. Failure to receive drugs (92 cases, 50.27%) accounted for the maximum MRHA, followed by ADRs (85 cases, 46.44 %) and overdose (6 cases, 3.27%). We were not able to identify any admissions due to other MRPs. The average cost associated with MRHA was found as INR 10,440 (USD-174, £- 149). ADR related hospital admissions imposed INR 8571 [USD-143, £-122 (Sd 4873.03)] on the patients. Failure to receive drugs resulted in a hospital charge of INR 12271 [USD-205, £-175 (Sd±8445.19)]. Overdose of drugs resulting in hospital admissions was associated with a cost of INR 8553 [USD-148, £-126 (Sd±3380.51)]. Age greater than 61 were identified as a risk factor for MRHA, and female gender was identified as a risk factor for ADR related hospital admissions.

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Conflict of Interest

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