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MEDICATION ERRORS IN EGYPTIAN CRITICALLY ILL PATIENTS WITH RENAL INSUFFICIENCY: AN ASSESSMENT OF THE NEED FOR OPTIMIZING CLINICAL PHARMACY SERVICE

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ABSTRACT: Background: The limited evidence of the critical role of clinical pharmacists in Egyptian teaching hospitals led to the fact that critical care pharmacists' responsibilities are still focused on dispensing and drug distribution. **Objective:** Assess the important role of clinical pharmacy service activities in an Egyptian intensive care unit (ICU) by describing the impact of medication errors on clinical outcome of critically ill-patients with renal insufficiency. **Methods:** An observational retrospective cohort study was carried out over a five months period on patients admitted to ICU with estimated creatinine clearance (CrCl) less than 50 ml/min on admission and known to have chronic kidney disease (CKD). Patient records, physician orders, pharmacy and nursing notes of 69 patients were collected and reviewed by a clinical pharmacist. Medication errors were assessed. Main outcome measure was Length of ICU stay and mortality. **Results:** One hundred and seventeen MEs were identified; prescribing errors (58.9%), wrong administration technique (17.9%), drug-preparation errors (11.9%) and monitoring errors (11.1%). Errors in renal dose adjustment were the most frequent prescribing errors (66.7%). The length of ICU stay was positively correlated with number of medication errors per prescription (r=0.392, p=0.001) and mortality was associated with significantly higher number of medication errors (p=0.01). Only 29% of errors observed were documented in pharmacy records and 93% of documented pharmacy interventions were accepted by the physicians. **Conclusion:** Decreasing morbidity and mortality in critically ill Egyptian patients with renal insufficiency may be achieved through optimizing clinical pharmacy services with prescription intervention activities.

INTRODUCTION: Medication errors (MEs) are major public health issues in hospitals because of their consequences on patients' morbidity and mortality [1, 2]. They are defined as a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient [3].

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Medication error rates in hospitals are higher in paediatric departments and intensive care units (ICUs) than elsewhere [4, 5]. Patients admitted to ICUs are at a high risk of MEs because of critical illness, complex ICU environment, multiple medications, and frequent changes in medication therapy.

Data from 205 ICUs in 29 countries found that the prevalence of MEs in ICUs was approximately 10.5 per 100 patient-days [5, 6, 7, 8]. Approximately one fifth (19%) of MEs in the ICU lead to life threatening events. Also, they lead to costly and prolonged hospital stays and some patients never fully recover to their premorbid status.

Moreover, patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) have an increased frequency of adverse safety events largely because of medication errors [7, 9].

The presence of clinical pharmacists in ICUs in countries with advanced clinical pharmacy services has reduced the number of adverse events, improved cost savings and medications, decreased mortality rates during ICU stay, and shortened the duration of ICU admission. Critical care pharmacists in those countries contributed greatly to patient safety and appropriate medication use [5, 6, 10-15]. However, less information is known about MEs and role of clinical pharmacists in Middle Eastern and African countries [16-18]. Moreover, studies addressing specifically MEs in ICU patients with renal insufficiency in Egyptian hospitals are lacking. In addition, the limited evidence of the critical role of clinical pharmacists in Egyptian teaching hospitals led to the fact that critical care pharmacists' responsibilities are still focused on dispensing and drug distribution.

Objective of the Study:

- Describe the frequency and type of medication errors and their impact on hospital stay and mortality in critically ill-patients with concomitant renal insufficiency at Critical Care Medicine Department- Cairo University Hospitals.
- Assess the need for optimizing clinical pharmacy service activities at the department to minimize medication errors and improve patients' outcome.

MATERIALS AND METHODS:

Study Population: Sixty-nine Egyptian patients were recruited during the period between August 2014 and December 2014. Patients were recruited from those who were admitted to the Critical Care Medicine Department, Cairo University Hospitals. All patients with estimated creatinine clearance (CrCl) less than 50 ml/min on admission and known to have chronic kidney disease were included into the study. Patients with shock and/or on dialysis were excluded.

Study Design: This was an observational retrospective cohort study. All patients fulfilling the inclusion criteria during the study period were recruited. Patient records, physician orders, pharmacy and nursing notes of 69 patients were collected and reviewed by a clinical pharmacist. Patients' demographics, laboratory investigations and physicians' notes were all recorded from patients' files. Medication errors found in physician orders and nursing notes were assessed and recorded for each patient. Medications needing dose adjustment in kidney dysfunction and potential nephrotoxic drugs were assessed along with estimated creatinine clearance. In addition, MEs that were detected, corrected through intervention and reported in clinical pharmacy notes were recorded. Creatinine clearance was calculated according to Cockroft-Gault equation using ideal body weight (IBW). For obese patients with weight greater than 30% over IBW, adjusted body weight was used instead of IBW [19, 20].

Ethics Approval: Due to retrospective nature of the study, ethics committee approval and consent form was waived by the Council of Critical Care Medicine Department.

Medication Errors: In this study, MEs were classified into prescribing errors, wrong administration errors, drug preparation errors and monitoring errors. Definitions pertaining to each of the MEs types are well documented in the international literature [3, 21, 22].

Statistical Analysis of Data: All data were analyzed using SPSS version 16 and graphics utilizing MS Excel. All continuous data were expressed as mean ± SD, while categorical data were expressed as frequencies. For comparative purposes between groups in all continuous data, independent t test was adopted. Pearson coefficient correlations were performed to assess the strength of the relationship between two variables. A P value of less than or equal 0.05 was considered to be statistically significant.

RESULTS: A total of 69 patients were included in the present study. The patients' demographics and clinical characteristics are shown in **Table 1**. Co-morbidities were present in all patients. The most frequent comorbidity was coronary heart disease, followed by hypertension and diabetes. During the study period, all recruited patients had at least one

medication error in their presciptions. A total of 117 MEs were identified; 69 prescribing errors were (58.9%), 21 wrong administration technique (17.9%), drug-preparation errors (11.9%) and monitoring errors (11.1%). In addition, prescribing errors were subdivided into incorrect instructions, lack of dose adjustment, significant drug-drug interactions and incorrect drug selection, **Fig. 1**.

TABLE 1: DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF THE RECRUITED PATIENTS

Variable	Values (N = 69)
Age, in years (Mean ± SD)	62.15±15.1
Gender distribution (Male %)	55.1
BMI, in kg/m^2 (Mean± SD)	29.07±5.24
Baseline CrCl, in ml/min	27.5±12.45
(Mean ± SD) *	34.8
Mortality (%)	10.39±7.5
ICU Stay (Mean ± SD)	

BMI: body mass index, CrCl: Creatinine clearance, ICU: intensive care unit, * CrCl calculated using Cockcroft-Gault Equation

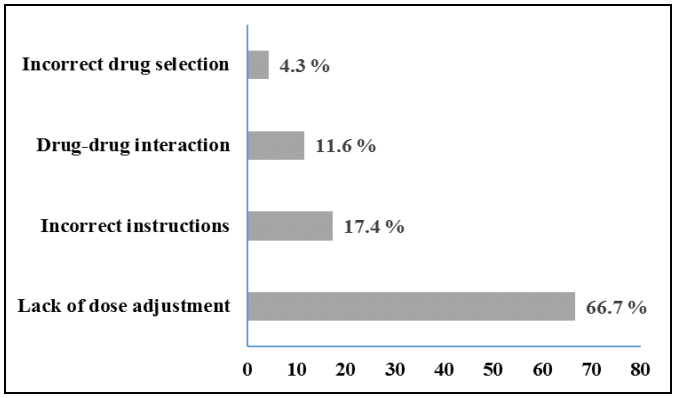

FIG. 1: PERCENTAGE OF PRESCRIBING ERRORS IN STUDY PATIENTS

Medications Associated with the most Frequent Medication Errors: Potential medications needing dose adjustment in kidney dysfunction were teicoplanin, meropenem, levofloxacin, fluconazole, ranitidine, piracetam, enoxaparin, digoxin and allopurinol. Amiodarone, warfarin, atorvastatin and fluconazole had the highest rate of drug-drug interactions. Omeprazole, vancomycin, teicoplanin and ranitidine were usually associated with wrong preparation technique due to incorrect instructions. Captopril, calcium salts, allopurinol and thyroxine were all associated with incorrect instructions regarding their administration with regard to meals. Lack of awareness of physicians that moderate adverse effects of drugs are aggravated when concomitant drugs with the same adverse effect are taken together, led to monitoring errors especially in electrolyte levels and QT monitoring (*e.g.* need for magnesium monitoring when using frusemide and omeprazole together). Physicians incorrectly selected domperidone to relief stomach discomfort in patients with heart failure and coronary artery disease without regard to its potential cardiovascular risk and to the significant drug-drug interactions with the QT prolonging drugs [23].

Effect of Number of Medication Errors on Length of ICU Stay: A positive significant correlation existed between the number of medication errors per patient and length of ICU stay, r=0.392, p=0.01. Moreover, medication errors due to lack of drug renal dose adjustment was significantly correlated with length of ICU stay, r=0.389, p=0.001).

Effect of Mean Number of Medication Errors on Mortality: Fig. 2 shows that mortality was associated with significantly higher mean number of medication errors. Similarly, **Fig. 3** shows that mortality was associated with higher mean number of medication errors due to lack of drug renal dose adjustment.

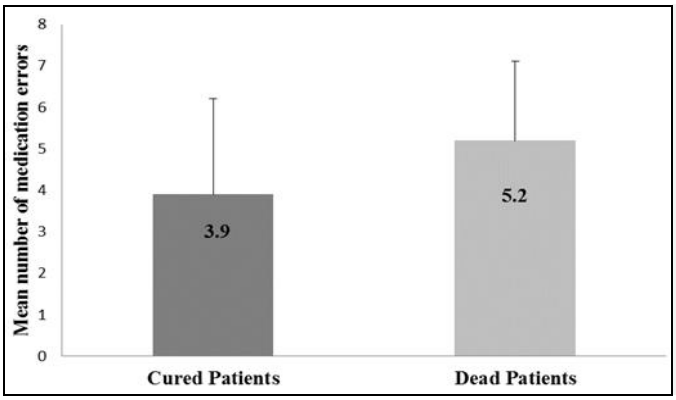

FIG. 2: EFFECT OF MEAN NUMBER OF MEDICATION ERRORS ON MORTALITY

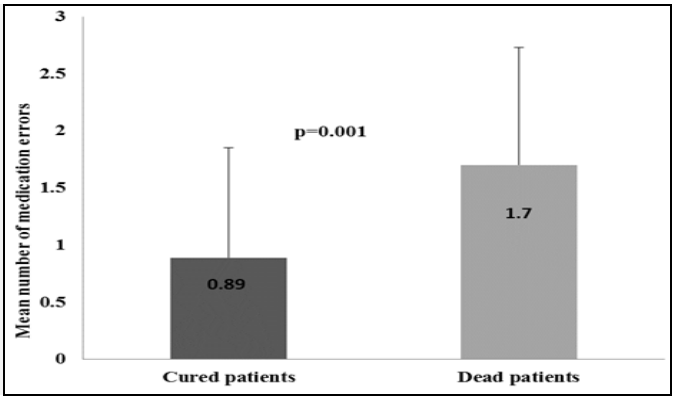

FIG. 3: EFFECT OF NUMBER OF MEDICATION ERRORS RELATED TO RENAL IMPAIRMENT ON MORTALITY

Role of Clinical Pharmacists: Total number of errors found in patients' file were 117 errors. Only 34 (29%) of those errors were detected and intervened by the critical care pharmacist. Physicians accepted 93% of pharmacist's interventions. Pharmacists records showed that interventions were usually made when clinical pharmacists had time to attend medical rounds. Clinical pharmacists interventions were: change drug dosage (38.2%), providing instructions regarding proper administration and reconstitution (29.4%), change time of drug dose with regard to meals (14.7%), monior crcl and/or electrolytes (11.8%), change time of drug dose with regard to another drug (5.9%).

DISCUSSION: Medication errors are important variable in determining patient safety [5]. They are among the most common preventable causes of adverse drug events. Relatively few studies of MEs in Egypt were conducted compared to the number from other Middle East countries, United States (US) and Europe [15, 17, 18, 24-28]. Moreover, MEs and role of clinical pharmacists in detecting medication errors and improving patient safety in ICU patients with renal insufficiency has never been addressed in an ICU of an Egyptian teaching hospital. The incidence of MEs is difficult to compare between studies because different methodologies and different definitions are used. However, according to Alsulami *et al*., errors could be classified according to where they occurred during the medication treatment process into prescribing, transcribing and administration [17].

In the present study sixty nine patient files were evaluated for presence of MEs. Hundred and seventeen MEs were detected. Prescribing errors were the most frequent MEs. This is in agreement with many studies conducted in Middle East countries [25-36].

In the present study, administration errors have been defined as a discrepancy between the drug therapy received by the patient and that intended by the prescriber or according to standard hospital policies and procedures [37, 38]. Our study showed that percentage of preparation and administration errors were 17.9% and 11.9% respectively. Fahimi *et al*., found that the error rates were higher in the administration process (66.4%) compared to the preparation process (33.6%) for intravenous medications, and within the administration process the technique of administration of bolus injection was the most common error (43.4 %) [39]. The higher percentage in the latter study compared to present study may be attributed to that their study was prospective. Our results indicate that the most common types of prescribing errors were lack of dose adjustment (66.7%), incorrect instructions (17.4%), drug-drug interactions (11.6%) and incorrect drug selection (4.3%). The results concerning lack of dose adjustment are consistent with previous studies' results [5, 40].

It is worth mentioning that in our study, 66.7% of physician orders required dose adjustment according to patient' renal function, 38.2% of which were adjusted by available clinical pharmacist. The latter intervention was the most frequent intervention made by clinical pharmacists. However, the 28.8% overlooked dosages necessitate the need for more pharmacist interventions.

Similarly, Stemer *et al*., conducted a systematic literature review on clinical pharmacy activities in chronic kidney disease and end-stage renal disease patients and found that the most common reported drug-related problems were incorrect dosing, the need for additional pharmacotherapy, and medical record discrepancies [41]. This is in accordance with Gidey *et al*., study conducted at an Ethipian hospital which found that dosing errors were common among patients with impaired renal function [42]. Also, a prospective cross-sectional study was carried out in the internal medicine wards of Tikur Anbessa Specialized Hospital to assess whether appropriate dosage adjustments were made in hospitalized patients with renal impairment.

The study results showed that dose adjustment was required in 31% of prescription entries and 51% prescription entries requiring dose adjustment were found to be inappropriate. The latter study concluded that improving the quality of drug prescription in patients with renal impairment could be of importance for improving the quality of care [43]. Moreover, as stated by Emami *et al*., drug dose

adjustment is a strategy that should be followed in order to individualize drug therapy and improve patient safety [44].

Similarly, Hassan *et al*., study in Malaysia reported that a renal drug dosing service for patients hospitalized with CKD by having a pharmacist accompanying the team of physicians on their rounds can increase the proportion of drug dosing that is adjusted to take into account renal function. The latter study stated that this can save drug costs and may prevent adverse drug events [45]. Moreover, Cabello-Muriel *et al*., study conducted at a Spanish hospital showed that a pharmacist intervention program improves the evolution of the renal function of hospitalised patient, especially in cases with stage 4-5 chronic kidney disease [46].

Our study showed that length of ICU stay correlated positively with number of medication errors. Moreover, mortality was associated with significantly higher mean number of medication errors. Similarly, mortality was associated with higher mean number of medication errors due to lack of drug renal dose adjustment.

Our study results is supported by previously published data which found that dosage adjustment based on renal function contributes to a reduction in the incidence of adverse drug events in older patients and others with renal impairment [45, 47].

The number of beds at our study ICU was 52 beds. Three pharmacists were fully occupied with non-clinical pharmacy activities and only one clinical pharmacist was available during the study period. However, the recommended ratio of critical care bed per one full time equivalent (FTE) clinical pharmacist according to the Society of Hospital Pharmacists of Austalia (SHPA) is 12 beds [48, 49].

Moreover, to allow critical care pharmacists sufficient time to perform their essential clinical duties, the Allied Health Professionals and the Healthcare Scientists Advisory Group in the United Kingdom (UK) recommend 0.05 to 0.1 full-time equivalent Grade D pharmacist for every level 3 bed and every level 2 critical care bed [50].

Accordingly, based on our results, one of the main contributing factors to MEs in the studied Egyptian ICU is the deficiency in the number of clinical pharmacists. This resulted in that clinical pharmacists are not adequately performing their job in reviewing prescriptions, performing appropriate interventions and providing education to health care professionals. Our opinion is in agreement with Rudal *et al.,* who collected intervention data from 21 adult critical care units over 14 days and concluded that a clinical pharmacist is essential for safe and optimised patient medication therapy and that an extended and developed pharmacy service is expected to reduce errors. Moreover, they recommended that clinical pharmacy services should be adequately staffed to enable adequate time for prescription review and maximal therapy optimization [51].

In addition, Conroy *et al*., stated that clinical pharmacists play a significant role in delivering training and competency assessment to reduce prescribing errors [44]. The main limitation of this study is its retrospective nature. Accordingly, we couldn't categorize MEs based on National Coordinating Council for medication error Reporting and Prevention (NCC MERP) Index for Categorizing Medication Errors Algorithm due to incomplete data in some patients' files [22]. Moreover, we didn't assess other patients' factors which might have affected mortality and length of ICU stay [52].

CONCLUSION: Decreasing morbidity and mortality in critically ill Egyptian patients with renal insufficiency may be achieved through optimizing clinical pharmacy service. This can be accomplished by; availability of competent clinical pharmacists, separation between pharmacists responsible for dispensing activities and those responsible for clinical pharmacy activities; increasing number of support staff to minimise non-clinical activities being undertaken by clinical pharmacists; raising the awareness of medical staff including pharmacists of the important role of clinical pharmacy service activities; and developing educational programs by clinical pharmacists to raise the awareness of the nursing staff and junior residents regarding potentially harmful medication errors and their impact on patient safety.

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CONFLICT OF INTEREST: Authors declare they all have no conflict of interest.

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