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Original Research

Levels of agreement among clinical pharmacists on the impact of pharmaceutical interventions in Oman: A retrospective analysis

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Abstract

Objectives: Disagreement between health care providers on medication-related interventions can affect clinical outcomes. We aimed to study the outcomes and significance of clinical pharmacists' interventions and evaluate the levels of agreement between different clinical pharmacists on the impact of pharmaceutical interventions. **Methodology:** A retrospective study was conducted at a tertiary care hospital in Oman. The study included all documented interventions by clinical pharmacists for all categories of admitted patients that met the inclusion criteria. **Results:** The originator clinical pharmacists interjected to improve the efficacy of treatment in (58%, n=1740) of the interventions, followed by toxicity reduction (24%). The level of agreement in the clinical significance resulted in substantial Scotts' kappa (k) between the originator and the first reviewer, the first and second reviewers, and the second reviewer and supervisor (86%; k=0.77; P<.001), (77%; k=0.63; P<.001), (84%; k=0.77; P<.001), respectively. In terms of grading of clinical significance, the originator clinical pharmacists recorded moderate significance in 50% of the interventions, followed by major (30%), not applicable (8.4%), and minor (7.3%). The level of agreement in the clinical significance resulted in substantial Scotts' k between the originator and the first reviewer, and between the second reviewer and supervisor (82%; k=0.72; P<.001), (84%; k=0.77; P<.001), respectively. The level of agreement between the first and second reviewer was fair (55%; k=0.28; p<0.001). **Conclusion:** Clinical pharmacists' interventions have a crucial impact on patient safety, improving efficacy and reducing toxicities. Overall, there was a substantial agreement among clinical pharmacists on the clinical significance and grading of the interventions..

Keywords: clinical pharmacist; level of agreement; interventions; efficacy; toxicities

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INTRODUCTION

Several international societies and organizations recommend a multidisciplinary team approach healthcare and many of these entities recommend the involvement of clinical pharmacists.[1,2] Clinical pharmacists in multidisciplinary care teams play an integral part in ensuring the quality use of medicines, reducing medication errors, and enhanced patient outcomes.[3] Ample evidence supports the value of clinical pharmacists' interventions in cost savings, improving medication adherence and clinical outcomes including reduced hospital stay among

hospitalized patients as well as reductions in hospital re-admissions.[4-9]

Disagreement between health care providers on medication-related problems or pharmaceutical interventions can lead to several adverse clinical outcomes, including; sub-optimal treatment, drug toxicities or increased overall healthcare cost.[10,11] A more recent study, showed poor overall agreement on the severity of clinical pharmacist interventions by other different health care providers in the team.[12] A study on asthmatic patients' management reported that physicians favored increased pharmacist involvement after reviewing their interventions.[13] Similarly, rheumatologists' agreement on variety of clinical pharmacists' interventions has led to encouraging trust in clinical pharmacists.[14] However, the levels of agreement between pharmacists with different experiences on the clinical significance and the grading of the clinical significance of medications related to pharmacists' interventions is scantly reported.

We aimed to study the outcomes and the significance of clinical pharmacists' interventions and to evaluate the levels of agreement between different clinical pharmacists on the impact of pharmaceutical interventions characterize the clinical pharmacists' interventions at Sultan Qaboos University Hospital (SQUH) in Oman.

METHODOLOGY

Study design, setting and population

This was a retrospective study conducted at SQUH, a tertiary care hospital in Oman, over 9 months from 1st January 2021 to 30th September 2021. At SQUH, clinical pharmacists work with various clinical teams in the wards and units, including; acute medical, intensive care, surgical, obstetric and gynecological, and pediatric services. Their interventions are documented on a specific form incorporated in the electronic patient record (EPR).

We retrieved all the recorded interventions by 14 clinical pharmacists over the study period. Complete intervention forms that contained free text information explaining the intervention details and stand-alone interventions (e.g., clinical pharmacist advice to take therapeutic drug monitoring (TDM) level for vancomycin) were included. Interventions that did not stand-alone without free text information and those with missing clinical or grading of clinical significance entries were excluded. We have collected the following data for each clinical pharmacist's interventions; the name of the admitting specialty, prescriber's designation, types and outcomes of the interventions, clinical significance, grading of the clinical significance, and the direct cost reduction associated with each intervention where applicable. We evaluated the interventions in a peer review process among the clinical pharmacists to validate their clinical significance and grading of the clinical significance.

Type of the interventions were classified according to The American College of Clinical Pharmacy Practice-Based Research Network Medication Error Detection[15] that included; ordering and prescribing error (e.g., availability, therapeutic duplication, formulation, addition, deletion, restricted/reserved, contraindication, re-start drug, withhold, dose, frequency, duration, route intravenous (IV) to oral), timing, combination, administration, omission, order expiry, double order, selection, or interaction), monitoring or follow up (e.g., TDM request, TDM follow up, lab test, or adverse drug reaction (ADR)) and modified to include other interventions related to information given to doctors or nurses, referral to others specialties and others, if any.

Clinical pharmacists recognized the outcome of the interventions after discussion with prescriber or treating team and classified into: accepted, rejected, accepted with changes or unknown outcomes. Clinical significance of the interventions was classified according to the therapy's projected goal, includes; efficacy improved, efficacy reduced, toxicity reduced, unnecessary exposure avoided, or not known.

Grading of the clinical significance was demarcated according to a pre-defined five-point scale, in which clinical pharmacists would select according to clinical scenario and seriousness of the intervention into death, major, moderate, minor or suboptimal.[16] Death is an error that might cause a major permanent injury or organ damage if not intervened. major is an error that can lead to temporary injury, harm, increased hospital length of stay (LOS), readmission or morbidity and requires a major correctional treatment. Moderate and minor errors that may lead to moderate or minor injury or harm that require temporary simple treatment, respectively. While, suboptimal standard of care/practice includes interventions that are unlikely to cause any harm, yet lead to a better care/practice.[16,17]

Peer review process

The peer review process of each clinical pharmacist's intervention was a process created to validate all included interventions for their clinical significance, grading of the clinical significance, and the associated direct cost reduction, that was carried at three major steps by first and second clinical pharmacists' reviewers (B.H., S.G., E.L., N.H., F.B., N.S., S.J., N.S., S.H., B.S., E.S. and S.Z.) and a clinical pharmacist supervisor (J.S.). Each clinical pharmacist was assigned a group of interventions that were not originally produced by themselves, and the peer review process is described in details in (**Figure 1**).

Statistical analysis

Descriptive statistics were used to describe the data. For categorical variables, frequencies and percentages were reported. For continuous variables, mean and standard deviation were used to summarize the data. Scott's kappa (κ) was used to assess the degree of agreement between the different clinical pharmacists, and to assess whether the degree of agreement was due to chance or a defined significant agreement.[18] The levels of agreements as well as Scotts' κ were presented along with their 95% confidence limits. The

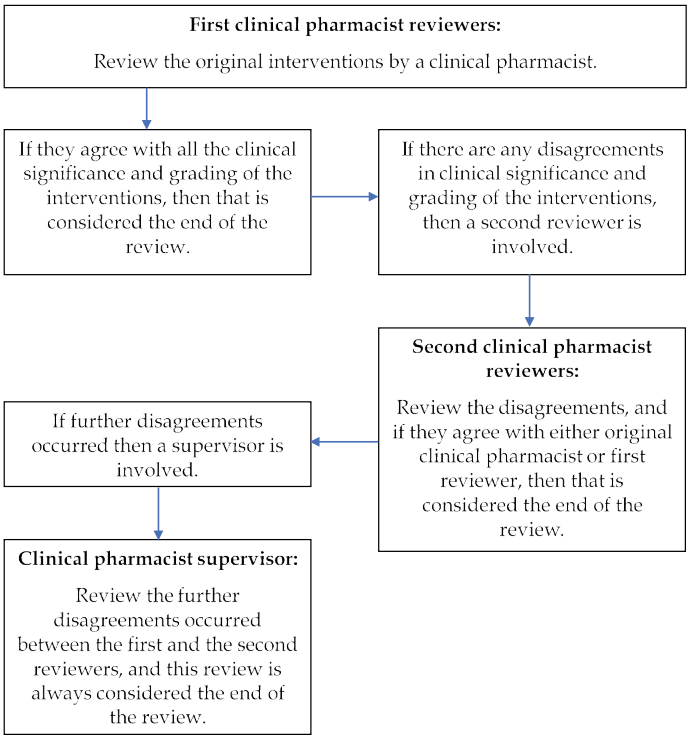

Figure 1. Peer review process by the clinical pharmacists

Scotts' κ values were interpreted by the following categories: poor agreement (κ < 0.01), slight agreement (κ = 0.01–0.20), fair agreement (κ = 0.21–0.40), moderate agreement (κ = 0.41–0.60), substantial agreement (κ = 0.61–0.80) and almost perfect agreement (κ = 0.81–1.00).[19] An a priori two-tailed level of significance was set at 0.05. Statistical analyses were conducted using STATA version 16.1 (STATA Corporation, College Station, TX, USA).

Ethics approval

The study was approved by the Medical and Research Ethics Committee at the College of Medicine and Health Sciences, Sultan Qaboos University, Muscat Oman (MREC #2657; SQU-EC/648/2021; dated: 14th December 2021). The study was also performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Data was anonymously stored and coded.

RESULTS

A total of 4,760 interventions were documented by 14 pharmacists for 24,075 admitted patients during the study period. After excluding those with missing information (n = 1,664), the final cohort for this study was 3,006 interventions, as outlined in **Figure 2**. The overall mean age of the patients involved was 50 ± 25 years old and 56% (n = 1694) were males. Adult medicine and adult intensive care unit (ICU) were among the highest clinical specialties involved in the interventions recorded, 44% (n = 1325) and 14% (n = 425), respectively. Around half of the interventions (46%; n = 1380) were discussed with residents/registrars/senior house officers, while 19% (n = 573) were discussed with intern doctors and 12% (n = 358) with senior specialists/specialists (**Table 1**).

Cardiovascular medications (23%; n = 693) and antibiotics (23%; n = 683) were among the highest type of medications recorded in our interventions (**Table 2**). Different types of clinical pharmacists' interventions are presented in **Figure 3,** with dose change (27%; n = 816), addition (16%; n = 489) and deletion (12%; n = 346) as predominant types. Almost 18% (n = 538) of the cases had ≥2 types of pharmaceutical interventions.

Table 3 present the outcomes of clinical pharmacists' interventions as discussed with the treating physicians in which the majority of the interventions were accepted (76%; n = 2,292), some were accepted with changes integrated (19%; n = 558) and only the minority was rejected (1.9%; n = 54). As a result, 970 (32%) interventions directly reduced the total cost

Table 1. Characteristics of patients involved in the interventions (N = 3006)

Age	
Mean±SD, years	50 ± 25
Range	1 day – 104 years
Age ranks, n (%)	
≤12	289 (9.6%)
13-18	134(4.5%)
19-64	1524 (51%)
≥65	1059 (35%)
Gender, n (%)	
Male	1694 (56%)
Female	1312 (44%)
Clinical specialties, n (%)	
Adult medicine	1325 (44%)
Adults intensive care unit	425 (14%)
General pediatrics	107 (3.6%)
Adult surgery	160 (5.3%)
Pediatric hematology	79 (2.6%)
Pediatric surgery	9 (0.3%)
Adult hematology	107 (3.6%)
Obstruction and gynecology	33 (1.1%)
COVID-19 team	44 (1.5%)
Unknown/Not recorded	723 (24%)
Physician designation, n (%)	
Senior consultant /Consultant	382 (13%)
Senior Specialist /Specialist	358 (12%)
Resident/Registrar/Senior House Officer	1380 (46%)
Intern	573 (19%)
Not specified	313 (10%)

SD, standard deviation.
Percentages might not add up to 100% due to rounding off.

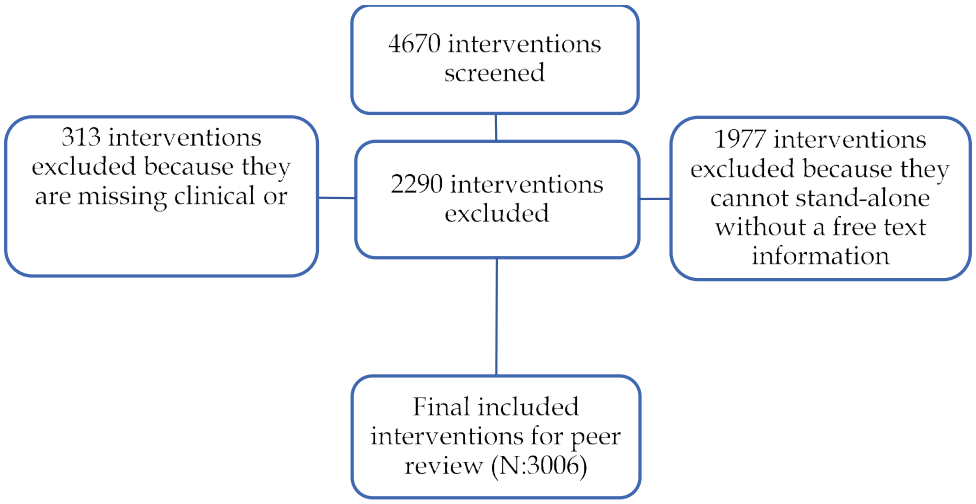

Figure 2. Inclusion and exclusion criteria for the peer review process

Table 2. Drug classes involved in the interventions (N = 3006)	
Drug class	**Frequency n (%)**
Cardiovascular system	693 (23%)
Antibiotics	683 (23%)
Endocrine system	363 (12%)
Gastrointestinal system	254 (8.4%)
Central Nervous system	235 (7.8%)
Nutrition and Metabolic disorders	232 (7.7%)
Analgesics	160 (5.3%)
Anti-infectives	106 (3.5%)
Blood disorders	83 (2.8%)
Respiratory system	73 (2.4%)
Cytotoxic drugs/ immunosuppressants	45 (1.5%)
Musculoskeletal system	26 (0.9%)
Eye preparations	15 (0.5%)
Skin preparations	14 (0.5%)
Genito-urinary system	13 (0.4%)
Vaccines	7 (0.2%)
Anesthetics	4 (0.1%)
Percentages might not add up to 100% due to rounding off.	

Table 3. Outcomes of clinical pharmacists' interventions (N = 3006)	
Interventions' outcome	**Frequency (%)**
Accepted	2292 (76%)
Accepted with changes	558 (19%)
Unknown outcome	65 (2.2%)
Rejected	54 (1.9%)
Not recorded	37 (1.2%)
Percentages might not add up to 100% due to rounding off.	

of the actual medication.

Levels of agreement in the outcome of the clinical significance of the interventions by the different clinical pharmacists is presented in **Table 4**. The level of agreement between the originator clinical pharmacists and the first reviewer was substantial, at 86% (95% confidence interval (CI): 85% - 88%) while the corresponding Scotts' k was 0.77 (95% CI: 0.75-0.79; P < .001). Furthermore, the level of agreement between the first and second reviewers was also substantial, at 77% (95% CI: 67%-88%) with Scotts' k at 0.63 (95% CI: 0.52-0.74; P < .001). Additionally, the level of agreement between the second reviewer and the supervisor was also substantial, at 84% (95% CI: 44%-100%) with Scotts' k at 0.77 (95% CI: 0.35-1.00; P < .001).

Lastly, as shown in **Table 4**, with regards to the grading of clinical significance, the level of agreement between the originator clinical pharmacists and the first reviewer was substantial, at 82% (95% CI: 81% - 83%) with the corresponding Scotts' k as 0.72 (95% CI: 0.70-0.74; P < .001). There was however, only a fair agreement (55%; 95% CI: 48%-63%), between the first and second reviewers with Scotts' k at 0.28 (95$ CI: 0.19-0.37; P < .001). Additionally, the level of agreement between the second reviewer and the supervisor was also substantial, at 84% (95% CI: 62%-100%) with Scotts' k at 0.77 (95% CI: 0.54-0.99; P < .001).

DISCUSSION

This study reported that cardiovascular medications and antibiotics were among the highest intervened class of medications. This study also identified a high proportion of dose change types of interventions with a high acceptance rate by the treating physicians. To our knowledge, no studies have focused on the agreement between pharmacists with different experiences on the clinical significance of pharmaceutical interventions. Our results demonstrated a substantial agreement between different pharmacists on the

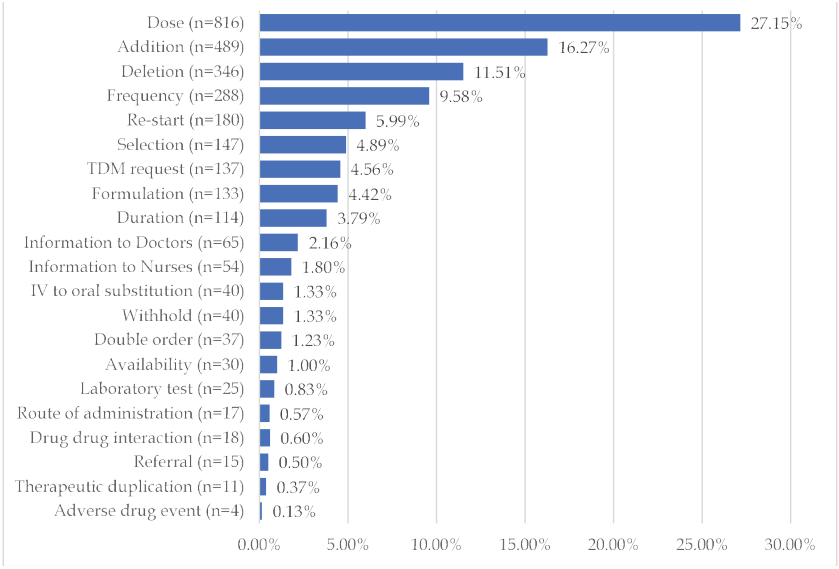

Figure 3. Types of clinical pharmacists' interventions (N = 3006)

Table 4. Level of agreements in the outcome and grading of clinical significance of the interventions by the different clinical pharmacists

Outcome	**Clinical Pharmacists**			
	1 (originator) (N = 3006)	**2 (1st reviewer) (N = 3006)**	**3 (2nd reviewer) (N = 253)**	**4 (supervisor) (N = 23)**
Clinical significance				
Efficacy improved	1740 (58%)	1641 (55%)	48 (19%)	5 (22%)
Efficacy reduced	10 (0.3%)	18 (0.6%)	0	1 (4.4%)
Toxicity reduced	725 (24%)	803 (27%)	119 (47%)	9 (39%)
Avoid unnecessary exposure	312 (10%)	372 (12%)	57 (23%)	7 (30%)
Not known	219 (7.3%)	172 (5.7%)	29 (12%)	1 (4.4%)
Level of agreement (2 vs 1); Scott/Fleiss' kappa p-value		86% [85% - 88%]; 0.77 [0.75 – 0.79]; p<0.001		
Level of agreement (3 vs 2); Scott/Fleiss' kappa p-value			77% [67% - 88%]; 0.63 [0.52 – 0.74]; p<0.001	
Level of agreement (4 vs 3); Scott/Fleiss' kappa p-value				84% [44% - 100%]; 0.77 [0.35 – 1.00]; p<0.001
	1 (originator) (N = 3006)	**2 (1st reviewer) (N = 3006)**	**3 (2nd reviewer) (N = 366)**	**4 (supervisor) (N = 57)**
Grading of clinical significance				
Death	16 (0.5%)	4 (0.1%)	1 (0.3%)	0
Major	894 (30%)	665 (22%)	83 (23%)	16 (28%)
Moderate	1510 (50%)	1663 (55%)	178 (49%)	25 (44%)
Minor	184 (6.1%)	266 (8.9%)	30 (8.2%)	4 (7.0%)
Not applicable	251 (8.4%)	208 (6.9%)	44 (12%)	12 (21%)
Suboptimal	151 (5.0%)	200 (6.7%)	30 (8.2%)	0
Level of agreement (2 vs 1); Scott/Fleiss' kappa p-value		82% [81% - 83%]; 0.72 [0.70 – 0.74]; p<0.001		
Level of agreement (3 vs 2); Scott/Fleiss' kappa p-value			55% [48% - 63%]; 0.28 [0.19 – 0.37]; p<0.001	
Level of agreement (4 vs 3); Scott/Fleiss' kappa p-value				84% [62% - 100%]; 0.77 [0.54 – 0.99]; p<0.001
Percentages might not add up to 100% due to rounding off.				

clinical significance and the grading of clinical significance of the studied pharmaceutical interventions.

This study showed that cardiovascular medications (23%) were among the highest class of medications recorded in our interventions. It was evident that clinical pharmacists play a significant role in improving cardiovascular medication use via related pharmaceutical interventions and medication reconciliation that led to significant health cost reduction.[14] Antibiotics related interventions were also high (23%) and this is in line with several other published studies,[20-22] which is highly assuring/supporting the role of clinical pharmacists as essential members of the antimicrobial stewardship teams.[16,23-27] Furthermore, results showed that dose changes due to suboptimal or supratherapeutic regimens were the primary type of interventions amongst others (27%), and this finding has also been reported elsewhere.[28-32] Interestingly, our study disclosed a high acceptance rate of up to 95% when combining both accepted and accepted with changes interventions, which is in line with the available evidence from systematic reviews and other observational studies.[22,29,33-35] We recommend the involvement of clinical pharmacists as an essential part of the multidisciplinary team in the management of patients.

There was a substantial agreement between different reviewers in their assessments of the clinical significance of the interventions. These results were in line with Bech et al. reported that the panelists agreed moderately in their drug-related problems (DRP) assessments of higher clinical relevance (κ = 0.5).[12] However, our findings were in contrast to those reported by Bosma et al. where the agreement between raters was poor for both the severity error or DRP and the value for service (weighted κ = 0.3 and κ = 0.2; respectively).[36] Similarly, poor overall agreement on the severity of DRP was found among panelists assessing pharmacists' interventions in elderly patients with chronic non-cancer pain (κ = 0.12)[12] and patients with rheumatic conditions (κ =0.29).[14] Unlike in our study in which the reviewers were clinical pharmacists, these studies involved different professionals in the rating process including an internal medicine specialist,[36] a rheumatologist[14] or a general practitioner.[12] In general, the internal medicine specialist rated the clinical relevance of the interventions lower than the hospital pharmacists.[36] The difference in rating between physicians and pharmacists was noted in studies related to ADR risk assessment, where there was a low agreement on the preventability of ADRs detected in hospitalized elderly patients (κ = 0.48).[37] Additionally, the difference in findings can be explained by the types of interventions analyzed, as our study included interventions that originated in a diverse range of specialties whereas other studies included interventions reported in a single specialty; internal medicine or rheumatology.[14,36]

The retrospective nature of this study limits its interpretation and generalizability. Furthermore, the study also excluded other major interventions due to the lack of information and missingness. Additionally, the peer review process design did not classify the groups based on the seniority of the clinical pharmacists' reviewers, for which only a small proportion of interventions reached the second reviewers and supervisor level.

CONCLUSION

Clinical pharmacists' interventions have a crucial impact on patient safety. Anticoagulants and antibiotics were among the highest recorded medication class of the interventions over the study period. The current study indicates that the clinical pharmacist interventions can improve the efficacy and reduce the toxicities associated with prescribed medications. Anticoagulants and antibiotics were among the highest recorded medication class of the interventions over the study period. Overall, there was a consistent substantial agreement among clinical pharmacists on the clinical significance of the interventions and their grading.

FUNDING STATEMENT

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CONFLICTS OF INTERESTS

All authors declared no conflicts of interest.

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