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RESEARCH ARTICLE

Polypharmacy as the risk factor of potentially inappropriate medication and medication regimen complexity index in hospitalised elderly patients

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Keywords
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Abstract

Background: The majority of elderly patients often receive complex therapy or polypharmacy due to physiological changes, which can develop into an adverse drug event. **Objective:** To analyse the risk factors of potentially Inappropriate Medications (PIMs) and medication regimen complexity in elderly patients. **Method:** This is an observational study with cohort retrospective methods, carried out at the In-patient Unit of Airlangga University Hospital, Surabaya. The inclusion criteria were patients aged ≥ 60 years old who were admitted between January to December 2019 for at least three days and received at least one drug. PIMs were monitored with Beers Criteria 2019 and therapy complexity was measured with Medication Regimen Complexity Index (MRCI) during admission, hospitalisation, and discharge. **Result:** Among 357 patients, 60.8% received at least one PIM on admission. Furthermore, the MRCI score decreased from 22.7 at the time of admission to 11.5 on discharge. Patients who received polypharmacy were two to three times more at risk of having PIMs ($p < 0.001$). The number of medications correlated with the MRCI scores (Correlation Coefficient= 0.815–0.877, $p < 0.001$). **Conclusion:** Polypharmacy is one of the risk factors of PIMs and medication regimen complexity, elderly patients who receive polypharmacy must be closely monitored to prevent adverse drug reactions.

Introduction

A complex therapy regimen or polypharmacy is unavoidable in elderly patients, and it is often influenced by several factors, such as age-related metabolic changes, multimorbidity, mental health conditions, and long-term treatment history (Dagli and Sharma, 2014; Rieckert *et al.*, 2018). Furthermore, it needs close monitoring due to the risk of adverse drug reactions (ADRs). A previous study was carried out to describe ADR, which occurred in hospitalised patients. The results showed that among 4,802 inpatients, 114 aged > 65 years experienced ADR at the time of hospitalisation (Giardina *et al.*, 2018).

Monitoring therapy in the elderly group can help to reduce the potential for medication errors. Several tools can be used for the process, including the Beers Criteria using the Potentially Inappropriate Medications (PIMs) as the output and Medication Regimen Complexity Index (MRCI) score as the result.

Beers Criteria is a tool often used to monitor the potential inappropriate medications in the elderly group, which must be avoided in certain situations or conditions (AGS Expert Panel, 2019). Meanwhile, the Medication Regimen Complexity Index (MRCI) is an instrument that can measure the complexity of a patient's treatment through several tables, including the dosage form of the drug, the number of doses per

day, and other additional instructions (George *et al.*, 2004)

The incidence of PIMs in elderly patients is associated with negative effects on health conditions and can affect the quality of life. It can also increase the risk of hospitalisation, drug-related problems, and other adverse health outcomes. Furthermore, PIMs are associated with an increase in healthcare costs (Alhawassi *et al.*, 2019). The complexity of therapy also occurs in elderly patients and causes several undesirable health conditions, such as ADR, poor quality of life, greater risk of being hospitalised, and lack of adherence to the therapy given by the prescriber (Osei *et al.*, 2016). Therefore, this study aims to analyse the PIMs and medication regimen complexity to prevent ADRs in hospitalised elderly patients.

Methods

Study design and participants

This is an observational study with a cohort retrospective method, and the data used were collected from August – October 2020. The inclusion criteria were elderly patients aged ≥ 60 years who were hospitalised at Universitas Airlangga Hospital between January and December 2019 and received at least one therapy with a three-day minimum length of stay. Patients who were transferred to a high-care unit referred to another hospital or died were excluded.

Data collection method

The non-probability method was used as the sampling method. Then, the minimum sample size is calculated by the Slovin formula and obtained a minimum number of samples of 40 samples per month. Data, such as therapy received by the patient at the time of admission, hospitalisation, and discharge were collected from the medication chart of elderly patients from January–December 2019. They were assessed based on the Beers Criteria 2019 and MRCI.

Variables

Independent variables include age (years), gender, length of stay (days), number of drugs (n), and comorbid (score), which was assessed using the Charlson Comorbidity Index. The Charlson Comorbidity Index (CCI), an assessment tool to predict long-term mortality, consisted of 19 items corresponding to different medical comorbid conditions. The total score of the CCI consists of a sum of the weights, with higher scores indicating a greater mortality risk and more severe comorbid conditions (Charlson *et al.*, 2022). While the dependent variables were PIMs (n) and MRCI scores.

Statistical analysis

Data normality was tested using the Saphiro-Wilk test. Analysis of the effect of the independent variable on the dependent variable during admission, hospitalisation, and discharge was performed using logistic regression for PIMs, and Spearman's correlation test for MRCI scores. The statistical analysis was carried out using IBM SPSS.

Results

In this study, 480 patients were randomly selected, but 123 were excluded. The final samples were 357 people, of which 52.40% were women (n=187) with an average age of 70 years (60 – 96 years). Most of the patients had respiratory (19.9%, n=71), endocrine (19.3%, n=69), and nervous (17.6%, n=63) system disorders. Furthermore, 52.1% (n=186) had a CCI score, which ranged from one to six. At the time of hospitalisation, 48.9% received four drugs (n=175), while 66.7% (n=238) were given five to nine in the hospital, and on discharge, most of them were administered with four drugs (75.4%, n=269), as shown in Table I.

Table I: Patient's characteristic

Characteristic		n (%)
Gender	Men	170 (47.60)
	Women	187 (52.40)
Age (years)	60-64	101 (28.29)
	65-69	78 (21.85)
	70-74	100 (28.01)
	75+	78 (21.85)
Comorbidity	0	171 (47.9)
	≥ 1	186 (52.1)
Length of stay (days)	≤ 8	346 (96.9)
	≥ 8	11 (3.1)
No. of drugs		
Admission, n (%)	≤ 4	175 (48.90)
	5 - 9	172 (48.30)
	≥ 10	10 (2.80)
Hospitalisation, n (%)	≤ 4	89 (25.00)
	5 - 9	238 (66.70)
	≥ 10	30 (8.30)
Discharge, n (%)	≤ 4	269 (75.40)
	5 - 9	87 (24.30)
	≥ 10	1 (0.3)
Prevalence of PIMs		

Characteristic		n (%)
Admission, n (%)	With PIMs	217 (60.80)
	No PIMs	140 (39.20)
Hospitalisation, n (%)	With PIMs	244 (68.40)
	No PIMs	113 (31.60)
Discharge, n (%)	With PIMs	182 (50.90)
	No PIMs	175 (49.10)
MRCI score Admission, mean (range)		22.70 (2–57.5)
Hospitalisation, mean (range)		27.89 (2–91)
Discharge, mean (range)		11.48 (2–28)

A total of 60.8% of the patients experienced PIMs which decreased at the time of discharge to 50.98%. The logistic regression showed that the number of drugs had a significant effect on its incidence at the time of admission (OR: 2.529, *p*-value < 0.001), hospitalisation (OR: 2.479, *p*-value < 0.001), and discharge (OR: 3,412, *p*-value < 0.001). Meanwhile, at the time of discharge, women were prescribed more PIMs than men (OR: 1.547, *p*-value of 0.041), as shown in Table II.

Table II: Logistic regression of determinants associated with PIMs in admission, hospitalisation, and discharge

Characteristic	Logistic regression					
	Admission		Hospitalisation		Discharge	
	OR	*p-value*	OR	*p-value*	OR	*p-value*
Gender						
Men	-	-	-	-	-	-
Women	1.170 (0.765–1.790)	0.469	1.180 (0.755–1.844)	0.467	**1.547*** **(1.018–2.349)**	**0.041***
Age (years)						
60-64	-	-	-	-	-	-
65-69	0.788 (0.431 – 1.443)	0.441	0.641 (0.344 – 1.194)	0.161	0.673 (0.371 – 1.218)	0.191
70-74	0.984 (0.555 – 1.746)	0.957	1.203 (0.648 – 2.231)	0.558	0.981 (0.564 – 1.708)	0.947
≥ 75	0.788 (0.431 – 1.443)	0.441	0.845 (0.448 – 1.595)	0.604	0.964 (0.534 – 1.743)	0.905
Length of stay						
≤ 8 days	-	-	-	-	-	-
≥ 8 days	0.768 (0.230 – 2.565)	0.668	0.545 (0.163 – 1.823)	0.324	0.796 (0.238 – 2.656)	0.710
Comorbidity						
0	-	-	-	-	-	-
≥ 1	1.102 (0.720–1.686)	0.655	1.060 (0.678-1.657)	0.798	0.867 (0.572-1.314)	0.501
No. of drugs						
≤ 5	-	-	-	-	-	-
≥ 5	**2.529*** **(1.633–3.916)**	**< 0.001***	**2.479*** **(1.509–4.075)**	**< 0.001***	**3.412*** **(2.014-5.782)**	**< 0.001***

*: Determinants statistically significant to PIMs

The MRCI score at the time of admission was 22.7, but it increased to 27.82 during hospitalisation and then decreased at discharge to 11.48. The correlation analysis during admission showed that comorbidity had a positive but weak relationship with the score (p = 0.016; r: 0.127), and the number of drugs had a strong positive correlation (p < 0.001, r: 0.841). During hospitalisation, the length of stay and comorbid have a weak positive relationship (p < 0.001, r: 0.232; p < 0.001, r: 0.227). However, the number of drugs has a strong correlation with the MRCI score (p < 0.001, r: 0.815). At the time of discharge, it also showed a strong positive correlation (p < 0.001, r: 0.879), as shown in Table III. The dosage form table had the strongest correlation and highest percentage with the MRCI total score.

Table III: Spearman correlation of determinants with MRCI score in admission, hospitalisation, and discharge

Characteristic	Admission	Hospitalisation	Discharge
	r (Sig.)	*r* (Sig.)	*r* (Sig.)
Age	-0.042 (0.430)	-0.024 (0.653)	-0.024 (0.653)
Gender	-0.073 (0.167)	-0.028 (0.600)	-0.028 (0.600)
Length of stay	0.076 (0.151)	**0.232 (<0.001)** *	**0.232 (<0.001)** *
Comorbid	**0.127 (0.016)** *	**0.227 (<0.001)** *	**0.227 (<0.001)** *
Number of drugs	**0.841 (<0.001)** *	**0.815 (<0.001)** *	**0.815(<0.001)** *

*: Determinants that statistically correlated to MRCI score

Discussion

The results showed that there was a decrease in the prevalence of PIMs (as shown in Table I). This finding is consistent with a previous study in which a total of 60 patients were evaluated, and 73% of them experienced at least one PIM on admission. Meanwhile, its prevalence during discharge was 50% (Chivapricha *et al.*, 2021). Another study was carried out to determine the rate of PIMs during admission in elderly Thai patients. The result showed that the total prevalence at admission was 43.3% (N = 187), while it reduced to 21.3% on discharge (Jo *et al.*, 2012).

There are several drugs in Beers Criteria 2019 given to patients, but metoclopramide was the most common drug. This finding is in line with a previous study, where it was received by 41.0% of patients (Masnoon *et al.*, 2017). In elderly people, metoclopramide can cause extrapyramidal syndromes, and the prevalence of adverse effects after its usage is 0.2% but can increase to 25% (Masnoon *et al.*, 2017).

The logistic regression result showed that the number of drugs (polypharmacy) affected the incidence of PIMs, which was defined as the use of five drugs or more (Abdullah *et al.*, 2018). This finding is consistent with a previous study, that 52% of patients experienced PIMs, and people with polypharmacy were 1.6 times more at risk compared to others. The results also showed that other variables did not have a significant effect on its incidence (Sharma *et al.*, 2020).

At the time of discharge, women had a 1.5-fold risk of developing PIMs compared to men. This finding aligns with a previous study, where they were 2.29 times more at risk (Faustino *et al.*, 2011). This is because women are more prone to chronic diseases, have more frequent visits to health facilities, and take medicines. They also have more detailed information related to their symptoms, which can increase the prescription given (Faustino *et al.*, 2011; Chang *et al.*, 2017; Al-Azayzih *et al.*, 2019).

The result showed that the MRCI scores increased at the time of hospitalisation because patients who were admitted to the hospital experienced worsening clinical symptoms. After the symptoms were reduced, the number of drugs administered also decreased.

A previous study was carried out to compare the MRCI scores at the time of admission and discharge from the hospital. The results showed that there was an increase in the average score from 28.7 at admission to 32.46 at discharge. This was caused by several factors, including the complex pre-admission therapy and the length of hospitalisation, which led to an increase in the number of drugs given (Pantuzza *et al.*, 2018).

A correlation analysis was performed to determine the relationship between MRCI scores and the independent variables. The number of drugs was the variable with the strongest association with the score. This finding is consistent with a previous study, where it also had a very strong relationship with MRCI (p < 0.001, r: 0.890) (Linnebur *et al.*, 2014). Comorbidities also showed a weak correlation with the scores, and this result is in line with another study, which obtained similar results (r: 0.22, p= 0.001) (Lee *et al.*, 2019). Furthermore, the length of stay also had a weak relationship with MRCI (p = 0.001, r: 0.242) (Negewo *et al.*, 2017).

It is important to note that the dosage form table had the highest percentage of the MRCI score, as shown in Figure 1. This finding is consistent with another study, where it accounted for 45.8% of the total value (Negewo *et al.*, 2017).

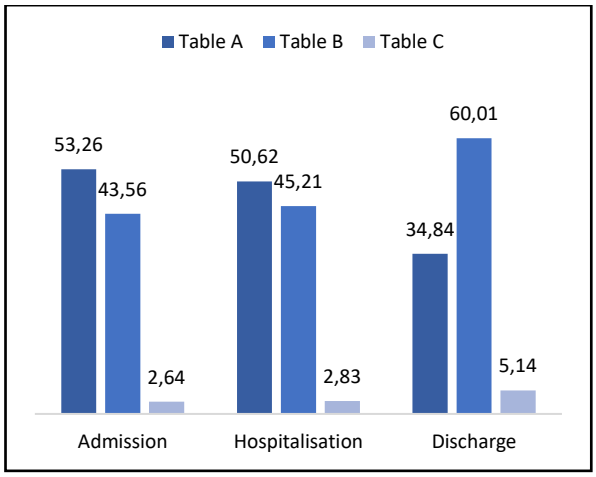

Figure 1: Percentage of each MRCI tables

Conclusion

The number of drugs and gender have effects on the occurrence of PIMs, while the number of treatments was a very strong correlating factor. Comorbidities and length of stay had a weak correlation with the MRCI score. Hence, elderly patients who receive polypharmacy must be closely monitored, and pharmacists must engage in interprofessional collaboration with other healthcare teams to prevent adverse drug reactions and improve patients' quality of life.

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