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Original Article

Rates, Variability and Associated Factors of Polypharmacy in Nursing Homes in Cyprus

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ABSTRACT

Background/Purpose: Polypharmacy is common in older people, particularly in those living in nursing homes and is associated with potential harms. This study aimed to assess the rates of polypharmacy and the factors related to it in a sample of nursing home residents in Cyprus.

Methods: We conducted a cross sectional study that included 8 nursing homes in the region of Limassol, Cyprus. Data recorded included: demographic characteristics, chronic medications, diagnoses and charlson comorbidity index (CCI) was calculated. Polypharmacy status was categorised in 3 groups: non-polypharmacy (0-5 drugs), polypharmacy (6-9 drugs) and excessive polypharmacy (≥10 drugs).

Results: 199 residents were included in the study; 135 (67.83%) were with dementia, out of which 71 were fully dependent (non-mobile). The mean age was 84.32 (*SD* 6.7). The average number of drugs prescribed was 6.06 (*SD* 2.91). Polypharmacy and excessive polypharmacy occurred in 39.7% and respectively 15.5% of the residents. Excessive polypharmacy was inversely associated with age ≥85 years (OR 0.43, 95 CI 0.2-0.90) and being demented (OR 0.38, CI 0.17-0.82). The most common drugs used were for gastrointestinal, neurological and cardiovascular disorders.

Conclusion: Polypharmacy is common among nursing homes residents in Cyprus, but excessive polypharmacy appears to be lower compared to other countries and presents significant variability. The community nursing homes, not-for profit, tend to have higher rates of excessive polypharmacy compared to private, for-profit nursing homes (18.90% versus 13.60%).

1. INTRODUCTION

Polypharmacy is the concomitant use of multiple medications. There is no consensus in the literature on the definition of polypharmacy, but the use of 5 or more drugs has become a widely accepted standard cut-off for clinical relevant polypharmacy while 10 or more drugs is often defined as excessive polypharmacy and is regarded as a pragmatic indicator of "high risk" prescribing.[1-3]

Polypharmacy is a well-known risk factor for adverse drug reactions, drug-drug interactions and low adherence to therapy, falls, hospitalisations and

increased healthcare costs.[4,5] For example, the Scottish Intercollegiate Guidelines Network (SIGN) on polypharmacy bring in attention that up to 11% of unplanned hospital admissions are attributable to harm from medicines and over 70% of these are due to elderly patients on multiple medications.[6] Moreover, numerous studies and systematic reviews reported polypharmacy as the main driving factor for potentially inappropriate medications use and potentially inappropriate prescribing (overprescribing, misprescribing and underprescribing).[7-9]

Older people living in nursing homes (NHs) are a paradigm of population with multimorbidities and polypharmacy. They have multiple chronic conditions, often with cognitive impairment and physical disabilities.[10-12] For example, a study conducted in Europe has found that 39.4% of residents in long-term facilities are dependent and 30.4% have severe cognitive impairment.[11]

The prevalence of polypharmacy in the long-term care facilities is high and varies widely between facilities, geographically location and definition used. It was found that up to 91%, 74% and 65% of residents take more than 5, 9, and 10 medications, respectively.[2] The European study SHELTER[11] which investigated the medication use among nursing homes residents in 7 European Union (EU) countries and one non-EU (Israel), found also high polypharmacy rates: 49.7% for 5-9 drugs and 24.3% for ≥10 drugs. Polypharmacy varied widely between countries and was directly correlated with comorbidities, depression and chronic pain, and inversely correlated with age, level of disabilities and cognitive impairment. In particular, Italy had the lowest prevalence of excessive polypharmacy (8.8%), followed by Israel (12.9%), Germany (15.7%), England (22.7%), the Netherlands (24.4%), Czech Republic (25.5%), France (30.2%) and Finland (56.7%).[11] Also, studies and national surveys in the United States, Canada and Australia have shown that prevalence of polypharmacy (≥9drugs) in the long term settings ranges between 15% and 40%.[13-15]

Despite all the interest in the topic, literature search showed no previous study of this kind in Cyprus. Given the increased risk of adverse health outcomes in older adults with polypharmacy and especially those taking ≥10 drugs/day, it is important to investigate which factors contribute to polypharmacy. Thus, the aim of this study was to investigate the degree of polypharmacy and the factors contributing to it in nursing homes in Cyprus.

2. METHODS

2.1. Study Design and Participants

This is a cross-sectional study that analysed the rate of polypharmacy and its possible associated factors in a sample of 8 NHs (six private, for-profit and two of community, not-for-profit) in the region of Limassol, Cyprus. The NHs in this region were approached sequentially and all those who agreed to participate were included in the study. Patient eligibility criteria included age ≥65 and being institutionalised for at least one month. Those terminally ill were excluded. Ethical approval was granted by the Cyprus National Bioethics Committee (Ref: ΕΕΒΚ ΕΠ 2019.01.65).

2.2. Data Collection and Measures

Data was collected from the medical files and discussion with nursing staff in each NH, from May 2019 to August 2019 and included age, sex, medication and comorbidities. We grouped the residents in the categories mobile and non-mobile according to the information given by nursing staff and in the categories residents with dementia and residents without dementia according to their diagnoses in the medical files. Only chronic prescribed medication (given for at least 1 month prior to data collection) that were given orally, injectable, by inhalation or eye drops were recorded and after that they were grouped into drug classes according to the anatomical therapeutic chemical (ATC) classification system (WHO, Collaborating Centre for Drug Statistics Methodology 2017). The drugs administered weekly (for example bisphosphonates) were taken into account. The charlson comorbidity index (CCI) was calculated for each patient. This index incorporates 19 diagnosis and predicts 10-year survival in patients with comorbidities in general population, while in the context of institutionalized elderly patients is a predictor of short-term mortality and, to a lesser extent of hospitalisation (the more points given, the more likely the predicted adverse outcome).[16] The included diagnoses are: myocardial infarction, chronic heart disease, cerabrovascular accident (CVA) or transient ischemic attack (TIA), peripheral vascular disease, dementia, chronic obstructive pulmonary disease (COPD), peptic ulcer disease, diabetes mellitus (DM), moderate to severe chronic kidney disease (CKD), hemiplegia, liver disease, solid tumour, leukaemia, lymphoma, connective tissue disease and acquired immune deficiency syndrome (AIDS). We determined 3 groups of polypharmacy, in lines with other studies: non-polypharmacy defined as 0-5 drugs/day, polypharmacy defined as 6-9 drugs/day and excessive polypharmacy defined as ≥10 drugs/day.[1,15,17] Taking into account that many of the residents in NHs are cognitive impaired and/or physically disabled, they were grouped as mobile or non-mobile and with dementia or without dementia.

2.3. Statistical Analysis

Descriptive statistics were used to describe patients' demographics and other variables. Means and standard deviations (SD) were used for continuous variables and proportions for categorical variables. The one-way analysis of variance (ANOVA) was used

for testing the relationship between continuous variables and categorical variables (in other words, comparing the mean number of drugs used between NHs). Logistic regression analysis (both binomial and multinomial where appropriate) was used to determine the independent variables affecting polypharmacy 6-9 drugs and excessive polypharmacy ≥10 drugs. A *p*-value of <0.05 was considered significant.

3. RESULTS

From the initial sample of 220 patients, those with missing data were excluded, leading to a final sample of 199, representing 71.32% of all residents in the eight NHs included in study. Mean age was 84.32 (*SD* 6.7) years, range 65-97 years, more than half (56%) been aged 85 and over and 140 (70.35%) were women. Table 1 shows the general characteristics of participants while Table 2 shows the characteristics of residents according to polypharmacy status and *p*-values.

The frequencies of non-polypharmacy ≤5 drugs, polypharmacy 6-9 drugs and excessive polypharmacy ≥10 drugs were 44.8%, 39.7% and 15.5% respectively. The mean number of drugs used per resident was 6.06 (*SD* 2.91) with a range of 0 to 14 and had a tendency to decrease with age, but the difference was not statistically significant (p=0.188). There were significant differences between the rates of polypharmacy and mean number of drugs between NHs, (p <0.05) ranging from 4.25 (*SD* 2.41) to 9.29 (*SD* 1.70). However, there were no statistically significant differences in polypharmacy rates between for-profit NHs and not-for-profit NHs (p=0.161; Table 3), but the latter had the tendency of higher rates of polypharmacy and excessive polypharmacy. Table 3 presents the rates of polypharmacy according to the type of NHs and Table 4 shows age, number of drugs and rates of polypharmacy in each of the specific NHs included in study. There were no differences between NHs in their mean age (p=0.133). Also, there were no differences in the rate of polypharmacy between residents grouped by sex (p=0.795) or between mobile and non-mobile patients' groups (p=0.845).

No differences in polypharmacy rate were found between mobile with dementia versus non-mobile (fully dependent) with dementia residents (p=0.127).

Table 5 shows the rates of main drug classes used in the sample where it can be seen that the most frequently used medications were H2 blockers/ proton-pump inhibitors, diuretics and angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs).

The mean CCI score was 5.54 (*SD* 1.3), without significant variations between NHs (p=0.85). The CCI score was positively associated with age (p <0.001, r=0.267) and number of drugs (p <0.001, r=0.393).

The logistic regression analysis showed two independent variables, inversely associated with excessive polypharmacy: age group ≥85 years (OR 0.43, CI 0.2-0.90), p <0.001 and having dementia versus without dementia (OR 0.38, CI 0.38-0.82), p=0.004.

Table 1. General characteristics of the participants in the study

General characteristics	Number of participants (%)
Gender	
Female	140 (70.35)
Male	59 (29.65)
Age	
65-74	19 (9.54)
75-84	68 (34.17)
≥85	112 (56.28)
Type of NHs	
Private	126 (63.3)
Community	73 (36.7)
Cognitive state	
With dementia	135 (67.83)
Without dementia	64 (32.17)
Mobility	
Non-mobile	86 (44.73)
Mobile	110 (55.27)

Table 2. Characteristics of participants according to polypharmacy status

General characteristics	Percent of drugs used by group			*P*-value
	0-5 drugs	6-9drugs	≥10drugs	
Age				0.032
• 65-74	4.00	5.10	1.70	
• 75-84	1.50	14.30	9.20	
• >85	31.51	25.79	6.88	
Sex				0.795
• Female	32.62	27.63	9.08	
• Male	12.06	12.06	6.53	
Cognitive state				0.031
• With dementia	32.66	27.63	7.53	
• Without dementia	12.06	12.06	8.04	
Mobility				0.845
• Non-mobile	20.6	17.08	5.52	
• Mobile	24.12	22.61	10.05	
Type of NHs				0.161
• Private	30.15	24.62	8.54	
• Community	14.57	15.07	7.03	
CCI score(mean+*SD*)	5 (1.12)	6 (1.27)	6 (1.62)	<0.001

Table 3. Rates of polypharmacy according to type of nursing NHs.

Polypharmacy status	Total	Private NHs	Community NHs
Non-polypharmacy <6	45%	48%	39.18%
Polypharmacy 6-9 drugs	39.7%	38%	40.54%
Excessive polypharmacy ≥10	15.5%	13.6%	18.9%

Table 4. Mean number of drugs, mean CCI score and rates of polypharmacy in 8 NHs

Nursing homes	Mean age (SD)	Mean number of drugs (SD)	Mean CCI score (SD)	Rate of non-polypharmacy ≤5	Rate of polypharmacy 6-9 drugs/day	Rate of polypharamcy ≥10 drugs/day
A	83.29 (5.06)	6.04 (2.82)	5.70 (1.57)	45.83	37.5	16.66
B	83.71 (6.32)	5.12 (2.09)	5.43 (1.19)	50	37.5	12.5
C	84.20 (6.32)	6.06 (3.66)	5.60 (1.49)	48.57	28.57	22.86
D	82.88 (8.60)	5.22 (2.28)	5.40 (1.09)	51.42	48.58	0
E	89 (3.46)	9.29 (1.70)	6.14 (1.06)	0	42.82	57.14
F	87.83 (3.88)	4.25 (2.41)	5.58 (0.99)	66.66	33.33	0
G	85.92 (7.83)	5.00 (2.48)	5.53 (1.12)	53.84	38.46	7.69
H	84.41 (6.77)	7.43 (3.00)	5.51 (1.43)	31.7	34.14	34.14

Table 5. List of main drugs classes

Frequencies of main drug classes	
H2 blockers and proton-pump inhibitors	44.22%
Diuretics	41.20%
ACE inhibitors and ARBs	39.19%
Neuroleptics	38.70%
Beta blockers	33.66%
Lipid lowering drugs	33.16%
Antiplatelet drugs	32.16%
Antidiabetic drugs	31.65%
Benzodiazepines	29.64%
Memantine and acetylcholinesterase inhibitors	27%
SSRIs and SNRIs	23.60%
Vitamins B complex	20%
Calcium blockers	19%
Antiepileptic drugs	15%
Acid uric lowering drugs	15%
Anticoagulants	12.56%
Ca +vit.D	12%
Alpha blockers	10%
Non-benzodiazepines sleeping drugs	10%
Multivitamins	10%
Anti-Parkinsonian drugs	7%
Levothyroxine	6.03%
Folic acid	6%
Nitrates	4%
Iron	3%

Abbreviations: ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; SSRIs, selective serotonin reuptake inhibitors; SNRIs, serotonin-norepinephrine reuptake inhibitors.

4. DISCUSSION

This study examines the proportions and factors related to polypharmacy and excessive polypharmacy in a sample of NH residents in Cyprus. Results suggest that the polypharmacy (6-9 drugs) is high, but comparable with other studies.[11,18] However, the excessive polypharmacy in this study (15.5%) appeared to be lower than the rate reported in other studies. In the European study SHELTER[11], conducted in 57 NHs in various European countries the excessive polypharmacy ≥10 drugs was 24.3%. A study conducted in Australia, 10 or more drugs were given to 26.5% of residents while the National Nursing Home survey conducted in USA indicated that 40% of residents used at least 9 drugs/day.[14,15] However, in the American survey almost 12% of the residents were <65 years old while in our sample none.

The variability of polypharmacy between NHs was high, excessive polypharmacy varying between 0% to 57.14%, this wide variability been also observed in other studies. In a Canadian study polypharmacy varied between 7.9% and 26.2% while in an Australian study the polypharmacy prevalence (≥9 drugs) varied even wider across facilities from 0% to 89%.[13,15] This wide variability has been attributed partially to the inclusion or exclusion of as-needed medications, topical formulations, vitamins, but also to different attitudes of prescribing physicians when facing the challenge of complex, multimorbid patients in NHs.[19] In addition, it may reflect the variability in the degree of disability and comorbidities between residents of different NHs. In our study sample there was no significant variation of CCI score between NHs, no difference in the mean age of patients between NHs and no differences in polypharmacy rate between mobile and non-mobile patients. However, in order to investigate the variability of polypharmacy is needed in-deep analyses of residents' characteristics and comparability between NHs; that could be the scope of future research. Moreover, private-for-profit NHs had lower rates of polypharmacy compared to public, not-for-profit NHs and this may indicate that organizational factors can play a role in the quality of drugs prescribing and that a decrease in medications is potentially feasible. However, in the literature the association between the type of NH and the likelihood of having higher polypharmacy rate is subject to conflicting results. Some studies showed similar results with ours, where private-for-profit NHs had lower levels of excessive polypharmacy compared to public NHs, while others found no differences in the polypharmacy rates related to the type of NHs.[17,18] On contrary, a study conducted in Belgium found that public NHs have lower medical consumption and expenditure.[20]

Some studies found an association between polypharmacy 6-9 drugs and functional abilities, but we did not find any association.[21] We found that increasing age and cognitive impairment is associated with a reduced rate of excessive polypharmacy. Regarding the age, other studies conducted both in NHs and in community also showed that being ≥85 years is protective factor against excessive polypharmacy.[22-24] In the same line, dementia was associated with a reduced rate of excessive polypharmacy, which is in concordance with other studies.[15,18,25,26] This may suggest a more cautious prescribing approach or even deprescribing for this group of frail older adults, which have limited life expectancy and therefore limited efficacy of pharmacological treatment and questionable appropriateness of treatment.[27] Also, cognitive impairment my cause communication difficulties including decreased ability to report pain or adverse effects.[23]

Regarding the pattern of main drug classes used, antiulcer drugs (H2 blockers and proton-pump inhibitors) were the most commonly used drugs followed by diuretics and ACEi/ARBs. Also, the use of psychotropic drugs was high, with 38.7% of residents receiving neuroleptics, 29.64% benzodiazepines and 23.60% antidepressants drugs. This distribution of drugs used in our sample of NHs is similar to other studies, but is worth noticing the high use of prescribed vitamins, 20% for vitamins B complex and 10% for multivitamins in our study, while for example, in SHELTER study only 4.1% residents took vitamin supplements.[11,18,26] We found surprisingly low use of analgesics, less than 1%, which may be explained by the fact that most of them were written as-needed and not properly recorded. We did not investigate the inappropriate prescribing, but systematic reviews indicate that almost one-half of NH residents are exposed to potentially inappropriate medications (PIMs).[8,9] It is worth noticing that the psychotropic drugs, which are highly used in our sample are leading cause of PIMs.[8,17,28] In addition, the proton-pump inhibitors which again, are highly used in our sample have been found in recent studies in USA to be prescribed in almost half of the residents without an evidence-based indication.[29]

Some limitations of the present study need to be recognised. Only 8 out of 34 NHs in the region of Limassol agreed to participate in the study and were included, therefore there may be a selection bias. However, because Cyprus is a small country with less than one million inhabitants and we included for-profit as well as not-for-profit NHs, we believe that our sample is representative regarding to age, sex distribution and clinical characteristics of Cyprus NHs residents. Second, unlike other studies investigating the polypharmacy, we did not take into analysis the length of stay and mode of feeding because the data regarding these two parameters were incomplete or unreliable. In addition, data collection was done by extraction from medical files and discussion with staff, not case by case ascertainment by discussing with the attending physicians and therefore we did not have information about symptoms or prescribing attitudes of physicians. Also, data collection from medical files were dependent on complete and accurate recording by physicians, which may have been incomplete.

5. CONCLUSION

In conclusion, the present study shows that polypharmacy is common in NHs in Limassol, Cyprus but excessive polypharmacy is lower compared to other countries. Longitudinal studies are needed to explore changes in polypharmacy rates and patterns of medications over time. Also, additional studies are required to investigate the clinical appropriateness of polypharmacy, the contribution of prescribing physicians and institution-related factors to the variability in polypharmacy.

CONFLICTS OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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Author Contributions

CI contributed to study design and planning, collected and interpreted data, performed statistical analysis, and drafted the paper. AJ contributed to study design and planning, provided input on data collection, analysis and interpretation, and finalised the paper. Both authors have approved the final submitted version.

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