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Polypill therapy and frailty in elderly: Time to stop treating everything

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ABSTRACT

Background: Frailty is a reversible age-related condition of increased vulnerability and risk of death or unplanned hospitalization. Frailty and polypill therapy are common in elderly, although little is known about the impact, they may have on each other. **Aims and Objective:** The study was a prospective observational study, designed with an aim to observe the six-month and one-year outcomes of elderly patients on polypill therapy. **Materials and Methods:** Three hundred forty-two patients aged more than 60 years on polypill treatment were enrolled in this study, which were on regular follow up in our rural hospital at geriatric units of medicine department. **Results:** At the end of one year, 38.1% were in severe frailty (FIRE >0.7) category, out of which death happened at the end of one year were 41.6%. 47.6% required repeated hospitalisations that were on polypill therapy. **Conclusions:** A reduction of polypill therapy could be a cautious strategy to prevent and manage frailty. Further research is needed to confirm the possible benefits of reducing polypill in the development, reversion or delay of frailty.

Key words: Elderly; Frail; Hospitalization; Mortality; Polypill

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INTRODUCTION

Frailty is a reversible age-related condition of increased vulnerability characterized by declines across multiple physiologic systems and associated with an increased risk of death or unplanned hospitalization. It is an emerging geriatric syndrome in clinical practice, and its associations include excess healthcare costs from consultations, polypill, and hospitalisation.[1] Frailty confers loss of independence in activities of daily living and dying when exposed to stress. There is current consensus that physical frailty is potentially reversible.[1,2]

Elderly people are often riddled with comorbid conditions and, as a result, become exposed to multiple drugs; this situation is often referred to as "polypill therapy". This is associated with a higher risk of adverse drug reactions and drug-drug interactions, moreover elderly patients often suffer from altered pharmacokinetics, reduced drug clearance, and cognitive deficits. Ultimately these patients are exposed to more hospitalization, hypoglycemia, high mortality and additional costs to the healthcare system.[3-5]

Various studies worldwide had shown prevalence of polypill in the elderly from 21% to 89%.[5-11]

According to last census, India is home to more than 100 million elderly people, still studies regarding the prevalence of polypill (for this investigation, defined as the concurrent use of ≥5 drugs) in relation to the covariates of comorbidity are lacking.[6-8] The main objective of this study was to predict all-cause mortality/ unplanned hospitalization with the aim of health promotion and

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disability prevention among older people who were on polypill treatments.

MATERIAL AND METHODS

This longitudinal observational study was carried out over a period of two years from January 2017 to December 2018 with patient follow up at one year. Three hundred forty-two elderly subjects more than 60 years were enrolled and studied, who were at regular follow up at our hospital in a program run by the institute, where Geriatric rural population are brought from remote rural areas, for the purpose of screening and treatment of for any illnesses or morbidities. The sample size was calculated by the formula: $n = Z^2 X(p) (1-p)/ c^2$; where n= Sample Size, Z = Z value (e.g., 1.96 for 95% confidence level), p = prevalence, c = confidence interval, expressed as decimal (e.g., .05 = ±5). Thus, sample will be: (1.96 x1.96) x 0.151(1-0.151)/ 0.05 x0.05 = 196.99. We had taken a sample size of 342.

Ethical clearance

The study received approval by the medical ethics committee of the University medical centre (Ref. no. DMIMS (DU)/IEC/2017-18/8359). Written informed consent was obtained from all study participants.

Electronic medical notes were used to gather patients' clinical and demographic information (including age, gender, admission diagnoses, number and types of comorbidities and the number of the prescription drugs on discharge).

Frail: The validated Kumar's FIRE-MED questionnaire helped in segregating the groups into frail, prefrail, and nonfrail categories.[8]

Polypill was considered as having 5 or more medications as per prescription.[9] Medication appropriateness for each patient was analyzed separately based on their medical history and clinical findings by applying the START (Screening Tool to Alert to Right Treatment) and STOPP (Screening Tool of Older Persons' Prescriptions) criteria.[9,10] Terminally ill and patients having serious cognitive disabilities that prevented comprehension and participation in the assessment were excluded from the study.

The primary end point of the study was overall survival. Mortality status was retrieved from telephonic contact with their relatives or registers of the municipalities where respondents were living.

Statistical Analysis was performed with help of Epi Info (TM) 7.2.2.2. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Means along with the standard deviations were calculated under descriptive analysis. Chi-square () test was used to test the association of different study variables. Multiple Logistic Regression analysis was performed to find the risk factors after adjusting the confounding factors. $p<0.05$ was considered to be statistically significant.

RESULT AND OBSERVATION

The mean age (± SD) of the patients was 67.47± 6.40 years, out of which 153 (44.74%) were between 60-65 years, 81 (23.68%) between 66-70 years, 72 (21.05%) between 71-75 years and 36 (10.53%) were more than 75 years. Out of 342 patient 50% were male and 135 (39.4%) were on polypill therapy. Other base line characteristics are shown in Table 1.

Out of 342 patients 27 (7.89%) were in fit frailty category (<0.25), 117 (34.21%) in mild frailty (0.3-0.4), 90 (26.32%) in moderate frailty (0.5-0.6) and 108 (31.58%) in severe frailty (>0.7) category. 41.66 % death happened in severe frailty (>0.7) category. Chi-square test showed that there was significant association between categories of Frailty Index Score and final outcome of the patients ($p<0.0001$). Prevalence of death was significantly higher among the patients with higher Frailty Index Score ($p<0.0001$) as shown in Table 2.

Table 1: Baseline characteristics

Characteristics	n = 342
Age, mean ± SD, years	67.47±6.40
Age, n (%), years	
60–64	81 (23.68%)
65–69	108 (31.58%)
70-74	63 (18.42%)
75 and above	90 (23.62%)
Gender	
Male, n (%)	171 (50%)
Female, n(%)	171 (50%)
Level of education, n (%)	
Illiterate	102 (29.8%)
Primary	207 (60.5%)
Higher secondary and above	33 (9.6%)
Number of comorbidities, median (IQR)	
Hypertension + IHD	163 (47.66%)
Neurological	145 (42.40%)
Cancer	145 (42.40%)
Diabetes mellitus	163 (47.66%)
COPD/asthma	172 (50.29%)
More than 3	81 (23.68%)
Hospitalization required	163 (47.66%)

Table 2: Distribution of patients according to frailty category

Frailty category	Number (N=342)	Deaths(n=72)
Fit (<0.25)	27 (7.89%)	0 (0%)
Mild Frailty (0.3-0.4)	117 (34.21%)	9 (7.69%)
Moderate Frailty (0.5-0.6)	90 (26.32%)	18 (20%)
Severe Frailty (>0.7)	108 (31.58%)	45 (41.66%)

Table 3: Multivariate Logistic Regression to find the predictive factors of death after adjusting confounding factors Unconditional Logistic Regression (Adjusted for age and other factors not related to FI score)

Variables in the Equation	Regression Co-eff. (β)	S.E.	Wald Static	df	p-value	Exp(β) (OR)	95% C.I. for EXP(β)	
							Lower	Upper
IHD	-17.880	1684.16	0.000	1	0.992, NS	1.716E-8	0.000	0.000
COPD	-1.844	0.515	12.827	1	0.0001, S	0.158	0.058	0.434
T2DM	-18.448	1661.34	0.000	1	0.991, NS	9.728E-9	0.000	0.000
Neurological	-1.276	0.520	6.033	1	0.014, S	0.279	0.101	0.773
Cancer	-1.379	0.000	.	1	.	0.252	0.252	0.252
co-morbidity more than 3	1.257	0.512	11.52	1	0.0001, S	0.351	0.251	0.356
Constant	40.189	2365.69	0.000					

Under the multivariable analysis, the results of logistic regression after adjusting confounding factors like age, gender, education and HTN showed significant predictive ability for death were Poly treatment in conditions like COPD, neurological studies and more than 3 comorbidities shown in Table 3.

DISCUSSION

Polypill therapy and frailty may be associated either ways, as frailty is linked to chronic diseases and multi morbidity, compelling general physician to prescribe multiple medications. There are several elements that may be considered clinical components or characteristics of frailty which are directly linked with the number of drugs taken, including weight loss, imbalance, generalized weakness, or functional deterioration.[11-14] Furthermore taking multiple drugs may be associated with an increase in drug vs drug interactions due to inappropriate prescribing and anticholinergic burden of treatments leading to more morbidity hence frailty.[15–18]

Longitudinal studies had reported a higher probability of becoming frail over time in patients with polypill.[19-21] Some study had found no association.[12] Those using more than seven drugs were at even higher risk. Wang et al. concluded that the risk of developing frailty increases with the number of medications taken.[20]

Polypill was indeed associated with an increase in comorbidities in our study as seen in other studies.[19,20] This can be explained by the need for more medications to address multiple comorbidities. It can also be explained by looking at comorbidity as the result of polypill, not only the cause of it.

Patients with ischemic heart disease and respiratory disorder were more on polypill, which may be justified as their management, require multiple medications. However, the older and frailer the patient, the more susceptible they are prone to multiple hospitalization due to various morbidity. Medications associated with blood pressure control, muscle fatigue, cramps, acid peptic disease like multiple antihypertensive drugs, statins and proton pump inhibitors may pose a higher risk for this group of elderly patients.[21,22] These findings were similar to those of other studies.[23,24]

The strength of our study is being the first study to examine the relationship between use of polypill therapy in elderly patients and its outcome which had been followed up for one year in India.

LIMITATIONS OF THE STUDY

A limitation of our study is that the analyses are based on data from just one tertiary care practice at rural setup. The duration of study is short to reach to a definite conclusion hence the cohort need to be followed further for definite association between frailty risk groups and polypill treatment.

CONCLUSION

Despite the obvious association, it is difficult to establish causality and determine what occurs first: frailty or polypill. Efforts should be made to improve medication use and minimize inappropriate polypill. Locally designed and delivered educational programs need to be implemented that can improve the awareness of general care practioners and beneficiaries such as elderly.

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Author's Contributions:
SK - Concept and design of the study; Interpreted the results; reviewed the literature and manuscript preparation; **PG -** Coordination, review of literature and manuscript preparation; **AG -** Statistically analyzed and interpreted; **SJ -** Preparation of manuscript and revision of the manuscript.

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