

# Polypharmacy- An Overview on the Challenges Faced by the Elderly with Cardiovascular Diseases

<sup>[1]</sup> Ishitta Sarkar

<sup>[1]</sup> Department of Biotechnology, Kanpur Institute of Technology, Dr A. P. J. Abdul Kalam Technical University, Lucknow, India

Corresponding Author Email: <sup>[1]</sup> 220495@kit.ac.in

**Abstract**— Demographic ageing has concluded for a growing multitude of aged people living with chronic diseases (multimorbidity) consuming five or more medicaments (polypharmacy) on an everyday basis. Ageing induces major differences in the cardiovascular system and represents the most dominant, potent single cardiovascular risk element. Cardiovascular diseases comprise of the greatest implications for the elderly, the healthcare systems and the caregivers involved throughout the process. Cardiovascular pharmacotherapy in the aged is complicated and burdensome because of age-related variations in body compositions, homeostatic mechanisms, organ functioning, and comorbidities enhances the pharmacokinetic and pharmacodynamic features of cardiovascular and non-cardiovascular drugs, which are in common use. Furthermore, polypharmacy results in an increased morbi-mortality and healthcare costs due to increased risk of drug interaction and its reaction. Lamentably, proof of drug efficacy and welfare of older citizens with multi morbidity and polypharmacy is restricted because these individuals are habitually excluded from clinical trials. In addition, clinical guidelines are written with a single- disease focus at large and only rarely addresses the issue of coordination of care, duration, and treatment discontinuation methodology, if required, or how to prioritize recommendations for patients with multimorbidity and polypharmacy.

This review scrutinizes the major challenges confronting healthcare professionals when prescribing in the elderly with CVD, multimorbidity, and polypharmacy. The objective is to impart information that can contribute to improving fragmented and siloed healthcare system and drug prescribing, early and accurate diagnosis of CVDs, as well as drug adherence and clinical outcomes.

**Keywords**— cardiovascular diseases, drug adherence, multimorbidity, pharmacokinetic.

## I. INTRODUCTION

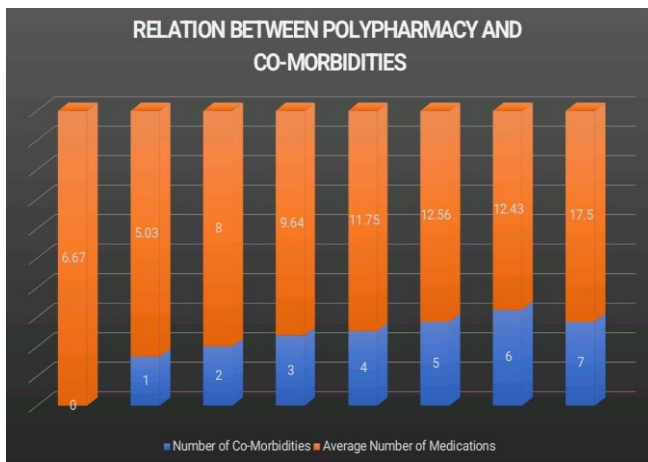
Polypharmacy is the concurrent use of multiple medications. Although there is no standard definition, polypharmacy is often defined as the routine use of five or more medications. This includes over-the-counter, prescription and/or conventional and complementary medicines used by a patient. Health care interventions are intended to benefit patients, but they can also cause harm. The nexus of processes, technologies and human interactions that constitutes the modern health care delivery system can bring notable benefits. However, it also involves an inevitable risk of patient harm that can – and routinely does – result in actual harm. Congruous polypharmacy is present, when (a) all medicines are advised for the purpose of achieving specific therapeutic objectives that have been agreed with the patient; (b) therapeutic objectives are actually being achieved or there is a reasonable chance they will be achieved in the future; (c) medication therapy has been enhanced to minimize the risk of adverse drug reactions (ADRs); and (d) the patient is motivated and able to take all medicines as intended (1). Inappropriate polypharmacy is present, when one or more medicines are prescribed that are not or no longer needed, either because: (a) there is no evidence-based indication, the indication has expired or the dose is unnecessarily high; (b) one or more medicines fail to achieve the therapeutic objectives they are intended to achieve; (c) one, or the combination of several medicines

cause ADRs, or put the patient at a high risk of ADRs or because (d) the patient is not willing or able to take one or more medicines as intended (1).

## II. UBIQUITY OF POLYPHARMACY

- A. *Multimorbidity*- It is defined as the presence of two or more long-term health conditions, which can include (a) defined physical and mental health conditions such as diabetes or schizophrenia; (b) ongoing conditions such as learning disability; (c) symptom complexes such as frailty or chronic pain; (d) sensory impairment such as sight or hearing loss; and (e) alcohol and substance misuse.
- B. *Facts and Estimated Data*- While its true magnitude is not known, the pervasiveness of polypharmacy is expected to rise due to a multitude of factors (2). First, the global population faces a demographic shift with the proportion of older population. It has been estimated that the global population aged over 65 years will double from 8% in 2010 to 16% in 2050 (3). In 2015, approximately 5% of the population in OECD countries were aged 80 years and above, this percentage is expected to rise more than double by 2050 (3). Second, epidemiological data showcases that multimorbidity increases markedly with age. In a Scottish study, multimorbidity was prevalent in 81.5% of individuals aged 85 years and over, with a mean number of 3.62 morbidities (4). Ornstein et al. found that the most prevalent chronic conditions in primary care were hypertension (33.5%), hyperlipidemia (33.0%), and

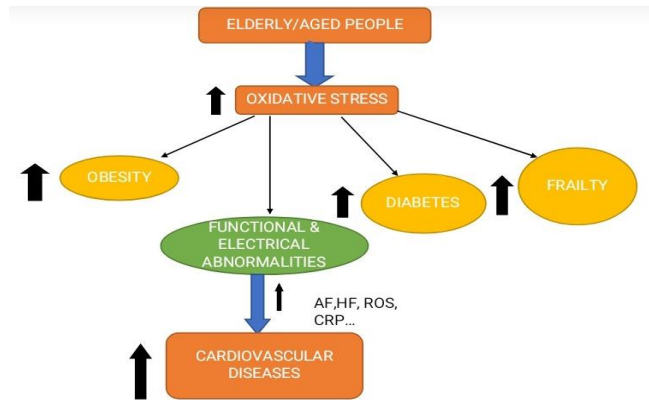
depression (18.7%) (5). The presence of multiple morbidities is associated with countless symptoms, impairments and disabilities. Multimorbidity may result in a combined negative effect on physical and mental health, and can have a major impact on a person's quality of life, limiting daily activities and reducing mobility (5). The need to take multiple medications can be just as problematic, resulting in recurring health care contacts and an increase in the plausibility of medication-related harm (6). Furthermore, it thrusts a large economic burden due to patients' complexity of health care needs and frequent interaction with health services, which may be fragmented, ineffective and incomplete.



Comorbidity refers to presence of more than one disease/condition in a person at the same time. This above graph showcases the co-relation between polypharmacy and co-morbidities.

### III. CARDIOVASCULAR DISEASES IN THE ELDERLY

In the aged people, we are dealing with increased frequency of cardiovascular diseases especially myocardial infarction, stroke, isolated systolic hypertension, calcific aortic stenosis, orthostatic hypotension, and syncopal attacks due to sick sinus syndrome, complete heart block, atrial fibrillation or other rhythm disorders. Alteration in cardiovascular status in the elderly has undesirable effects on their quality of life and longevity. Diagnosis of these disorders in the elderly requires special consideration since coexistence of structural/functional changes in the old age with cardiovascular disease would alter the classic features of these disorders and result in delay in their appropriate management. Biological aging as evaluated by reduced telomere length has a strong impact on the incidence of cardiovascular disorders especially coronary heart disease and chronic heart failure. This phenomenon could possibly explain interindividual susceptibility to cardiovascular disorders (7).



This above ray diagram describes the cause of high risk of CVDs due to age factor.

### IV. INTEGRATIVE TEAM APPROACH

Healthcare systems and clinical practice guidelines (CPGs) are mainly oriented towards single-disease rather than multimorbidity. (8) However, application of multiple disease-specific CPGs in patients with CVD and multimorbidity without integration may lead to contradictory recommendations and be impractical, or even harmful, and misaligned with patients' preferences and values. (9,10,11) Additionally, these patients are treated simultaneously by several specialists, which can lead to discrepancies in goals of care, drugs prescribed, and overall medical management. In these circumstances, a holistic patient care requires a multidisciplinary team for a successful comprehensive geriatric assessment and coordinated management of multimorbidity. The coordinated teamwork between the cardiologist and other medical specialists, nurses, pharmacists, social workers, family, and caregivers plays a key role in establishing the goals of cardiovascular pharmacotherapy according to the patient's preferences and values.

### V. PRESCRIBING MEDICINES TO OLDER PEOPLE—HOW TO CONSIDER THE IMPACT OF AGEING ON HUMAN ORGAN AND BODY FUNCTIONS

Older people face multiple problems potentially influencing the beneficial and adverse effects of pharmacotherapy, of which the actual effects are not always easy to predict beforehand. Prescribing (selecting, informing patients, initiating, monitoring and continuation) of drugs to older people provides major challenges to many physicians. Next to changes in pharmacokinetics and pharmacodynamics upon ageing, changes in body functions, such as visual acuity, motor functions and cognition also pose a challenge for appropriate prescribing as they may affect the correct use of the drug. To adequately address the needs of older people and their prescribers, it is important that during the drug development process sufficient information is gathered about the possible changes in pharmacokinetics and

pharmacodynamics in older people, especially in patients older than 75 years suffering from comorbidities, and that this aspect requires due consideration during drug authorization. Therefore, a revision of the ICH E7 criteria is recommended so that more data in people older than 75 years will be acquired. Furthermore, it is important during this process that any practical problems that older people may experience will be addressed by adjusting the product design. (12)

**VI. MAIN ADVERSE DRUG REACTIONS PRODUCED IN THE ELDERLY DUE TO FREQUENTLY PRESCRIBED CARDIOVASCULAR DRUGS**

The below illustrated [Table 1], describes some of the main drug types and their adverse consequences on the aged people due to commonly prescribed cardiovascular medications.

**TABLE 1. Drug category along with their main adverse effects**

DRUG TYPE	MAIN ADVERSE CONSEQUENCE
Glucose-lowering drugs	Aggressive glycaemic control ↑ the risk of hypoglycaemia, dizziness, confusion, and falls. Establish individual HbA1C targets balancing any benefits vs. hypoglycaemia risk.
Alpha-adrenergic blockers	Postural hypotension, especially in patients treated with diuretics or vasodilators. Dizziness, somnolence, and dry mouth.
ACEIs/ARBs	the risk of hyperkalemia, hypotension, falls, dizziness, fatigue, acute kidney injury, and cough (ACEIs)
Lidocaine	Tremor, dysarthria, altered levels of consciousness, nystagmus, and seizures
Antiplatelets	↑ risk of bleeding
Colchicine	Diarrhoea, nausea, vomiting, abdominal discomfort, and blood dyscrasias

**VII. A CORE ISSUE: DRUG ADHERENCE**

Medication adherence is a growing concern to clinicians, healthcare systems, and other stakeholders (eg. payers) because of mounting evidence that nonadherence is prevalent and associated with adverse outcomes and higher costs of care. (13) 30-75% aged population are not taking drugs that they are supposed to be taking. With increasing polypharmacy and multimorbidity rates, non-adherence also is on an increase and is in accordance with poor QoL, increased mortality rates and high medical costs. Systematic checking of drug efficacy and safety is critical to prevent ADRs and improve QoL and clinical outcomes. However, up to two-thirds of patients receiving cardiovascular drugs that require lab-based track (i.e., renin-angiotensin-aldosterone

system inhibitors, digoxin, glucose-lowering drugs, and warfarin) are not regularly monitored. (14)

**VIII. SIGNIFICANCE OF PERIODIC SYSTEMATIC MEDICATION REVIEWS**

For the enhanced clinical outcomes, vigilant planning of drug regimens is required.

<b>Identify all medications that the patient is currently using ("trust but verify")</b>
<ul style="list-style-type: none"> <li>Prescribed, OTC, HMPs, CAM and dietary supplements</li> </ul>
<b>Assess patients' co-morbidities, cognition, functional status, and social support</b>
<ul style="list-style-type: none"> <li>Review records: clinics, hospital, skilled nursing, assisted living, nursing homes</li> <li>Screen for diet and nutritional state</li> </ul>
<b>Define overall care goals</b>
<ul style="list-style-type: none"> <li>Based on functional status, QoL, estimated life expectancy and patients' preferences</li> <li>Primary/secondary prevention, acute/chronic treatment, symptom control/management</li> </ul>
<b>Match each medication with patients' condition and goals of care</b>
<ul style="list-style-type: none"> <li>Confirm that all prescribed drugs are indicated and effective*</li> <li>Consider to deprescribe ineffective, unnecessary, or repeated medications</li> <li>Replace any drug by a potentially safer and more effective alternative</li> </ul>
<b>Consider the need of new medications</b>
<ul style="list-style-type: none"> <li>Confirm whether all recommended drugs are prescribed</li> <li>Consider underlying causes to treat and the risk/benefit ratio</li> </ul>
<b>Document adherence and response to therapy</b>
<ul style="list-style-type: none"> <li>Assess whether the patient follows the treatment correctly: dosage, frequency, route of administration and duration</li> <li>Simplify the treatment: once daily, easy to swallow, medications with dual indications</li> </ul>
<b>Identify drug-related ADRs and drug-drug/drug interactions</b>
<ul style="list-style-type: none"> <li>Any new symptom/cognitive change should be considered an ADR until proven otherwise</li> <li>Evaluate the cause and severity and discontinue culprit drugs</li> <li>Assess liver and kidney function and adjust the dose accordingly</li> </ul>
<b>Provide drug information to patients and caregivers</b>
<ul style="list-style-type: none"> <li>Simple verbal/written instructions for every medication</li> <li>Explain the goals of treatment and the reasons to discontinue/initiate a new medication</li> </ul>
<b>Improve communication between health care providers</b>
<ul style="list-style-type: none"> <li>Information should be readily available to all caregivers</li> <li>Adopt a multidisciplinary care approach including GPs, pharmacists, nurses, dietitians, and other health care providers</li> <li>Communication between hospital and community care providers is essential</li> </ul>

(15)

The above medication review showcases a structured periodic review of all medications, matching each medication to the patient's comorbidities and objectives of care.

**IX. ISSUES OF PRESCRIBING FLAWED MEDICATIONS**

Improving prescribing for older people is an essential part of medical care and a priority for all healthcare systems. Inappropriate polypharmacy is a common practice and includes the prescription of medications when there is no evidence-based indication or the indication has expired; it fails to achieve the therapeutic goals and causes unacceptable ADRs when safer and/or more effective drugs are available or the patient is not willing or able to take the medicines as intended. (15,16,17)

Cardiovascular drug therapy optimization while avoiding the use of potentially inappropriate medications (PIMs) can enhance clinical outcomes and reduce ADRs. Several tools can help to identify PIM and/or potential prescription omissions in older people, including Beers, STOPP/START (Screening Tool of Older People's Prescriptions/Screening Tool to Alert to Right Treatment) criteria, EURO-FORTA (Fit for The Aged) list, and the Medication Appropriateness Index. (18,19,20) The ACOVE-3 (Assessing Care of Vulnerable

Elders-3) and GPGPA (Good Palliative-Geriatric Practice Algorithm) tools are useful in determining the need for medication continuation in vulnerable older adults who are closer to the end of life. However, no one validated tool assesses all aspects of PIMs or has been shown to be superior in improving patient-related outcomes and decreasing polypharmacy risks, and it remains unclear whether they reduce hospital admissions. <sup>(21,19,20)</sup> A simple and effective approach to systematically identify PIMs is to match each of the patient's conditions with their medications. (15)

## X. CONCLUSION

Major focus on the comprehensive assessment of the risk and complexity of prescribing cardiovascular drugs is necessary to ensure that aged people with CVD and multimorbidity receive the most effective and safest cardiovascular pharmacotherapy. This review talks about the ubiquity of polypharmacy, co-relation between polypharmacy and co-morbidity, an integrative team approach, drug adherence factor, importance of periodic systematic drug review, issues of prescribing flawed drugs, and the main adverse drug reactions produced in the elderly due to commonly prescribed cardiovascular medications. Hence, it is concluded that a congruous prescription of safe and effective pharmacotherapy in aged people with CVD and multimorbidity exists as one of the greatest ultimatums in geriatric medicine and dose adjustments are required to drastically reduce the risk of ADRs. Also, certain cardiovascular drugs should be administered with caution, avoided, or closely monitored when prescribed in the elderly. There is an urgent need to evolve appropriate and specific CPGs for this growing population based on RCTs (or consensus, until trial data become available) that confers how the most common comorbidities impact the applicability of guideline recommendations and prioritize the diagnosis and treatment that optimize benefits, improve physical and psychosocial function, QoL, and outcomes, and minimize harm (ARDs and DDIs) in this population. To sum up, better clinical evidence is always welcomed regarding the efficacy and safety of cardiovascular drugs in older people with CVD and multimorbidity.

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