

# Retrospective study of prescribing Cascade-A negative outcome of Polypharmacy

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## ABSTRACT

Even though medicines are used for their positive outcomes, it can produce hidden negative outcomes as well. Negative outcomes may lead to a condition where it is mistaken to be an indication for a new drug and even the second drug may produce other adverse events which in turn requires treatment and the chain prolongs leading to prescribing cascade. A retrospective study of one year duration was conducted in a secondary care hospital in southern India. Patients admitted under general medicine department during study period and satisfied inclusion and exclusion criteria were randomly selected. Patients aged  $\geq 18$  years and prescribed with more than one drug were included but Patients who got discharged against medical advice were excluded from study. A total of 261 patients were enrolled. 73(27.9%) patients were in the age group of 68-77. While correlating number of drugs prescribed and prescription cascade, it was found that adverse drug event as well as its direct influence on prescribing cascade increases with increase in number of drugs. Almost all patients in the study population with more than 10 drugs had prescribing cascade. Hence polypharmacy can be considered as a major risk factor for development of prescribing cascade. As adverse drug events are prevalent in our population especially in elderly and majority of these events are dose related, initiation of treatment with lowest effective dose, effective communication and reconciliation of all medicines prescribed by different health professionals caring for a patient is vital to curtail the prescribing cascade.

**Keywords:** Prescribing cascade, Polypharmacy.

## INTRODUCTION

Medicines being double edged swords have the potential to cause harmful adverse events. It places a significant burden on the healthcare system in terms of both health outcomes as well as cost. It has been estimated that 10% of patients visiting the general practitioners have had an adverse drug event in the previous six months<sup>1</sup>. Timely Recognition of adverse drug events and intervention to prevent further harm is a mandatory requirement to promote rational drug use. The condition will become more dangerous when the adverse drug event is mistaken to be an indication for a new drug and even the second drug may produce another adverse events then the chain prolongs to lead a prescribing cascade.<sup>2,3</sup>

A prescribing cascade occurs when a new medicine is prescribed to treat an adverse drug reaction associated with another medicine, in the mistaken belief that a new medical condition requiring treatment is present. Prescribing

casades may also occur when an adverse drug reaction is anticipated from the current treatment. An example is the prescription of pyridoxine to reduce peripheral neuropathy associated with the anti-tubercular drug Isoniazid. Prescribing cascades put the patient at further risk of harm though some may be recognized adverse reactions.<sup>3,4</sup>

Adverse drug events comprises of errors in the way the medicine is used, and adverse drug reactions that result from the pharmacological properties of the drug itself or genetic makeup of the host. Prescribing cascades can exacerbate the harmful effects of an unrecognized adverse drug reaction. Dry cough caused by angiotensin converting enzyme inhibitor may be considered as respiratory infection by mistake which in turn leads to prescription of an unnecessary antibiotic with the potential to cause severe diarrhea. Patients usually experience an adverse drug reaction within four months of starting a new drug, with 75% of these patients

experiencing the adverse drug reaction within one month.<sup>5</sup>

### METHODOLOGY

A retrospective study of one year duration was conducted in a secondary care hospital in southern India. Patients admitted under general medicine department during the study period and satisfied the inclusion and exclusion criteria were selected. Samples were randomized using Graphpad software. Patients aged  $\geq 18$  years and prescribed with more than one drug were included in the study. Patients who got discharged against medical advice were excluded from the study. Selected patients demographic details, past medical and medication history, treatment charts, progress notes and pertinent laboratory reports were collected and recorded in a pre-designed data collection form.

### RESULTS AND DISCUSSIONS

A total of 261 cases were enrolled in the study. The age group of subjects was convened into a frequency of 10 and table 1 illustrates the age distribution in the sample population (Table 1). Seventy three (27.9%) patients in the study population were in the age group of 68-77 from both genders. From this it can be concluded that elderly population are more affected by the adverse outcome from the treatment and the resulting prescribing cascade. Since the drug handling capacity of various organs in the body declines as the age progresses, identification and interruption of prescribing cascade is an important actionable and underappreciated opportunity to improve medication safety in elderly people.

**Table 1: Distribution of patients based on age and gender**

Age in years	Male	Female	Pooled	
			#	%
18-27	08	06	14	5.3
28-37	14	16	30	11.4
38-47	14	18	32	12.2
48-57	18	21	39	14.9
58-67	16	12	28	10.72
68-77	32	41	73	27.9
78-87	20	08	28	10.72
$\geq 88$	12	05	17	6.5
Total	134	127	261	100

Medical history of the patients were assessed and perceived that almost all patients had medical history of chronic diseases and about 6.5% patient's medical history was

unknown (Figure 1). A good number of participants (26.81% and 24.5%) of the study population were suffering from life style diseases like diabetes and hypertension respectively.

**Table 2: Medical History of patients**

Medical History	Male (n=134)	Female (n=127)	Pooled	
			#	%
Diabetes	38	32	70	26.81
Hypertension	30	34	64	24.5
Diabetes+Hypertension	23	11	34	13.0
Metabolic syndrome	18	08	26	09.9
Asthma/COPD	10	21	31	11.8
Thyroid disorders	05	14	19	07.2
Medical History NA	10	07	17	06.5

Figure 1 depicts the medical conditions of the study population. It is clear from the study results that majority of patients got admitted in the hospital for the management of their chronic diseases like hypertension and diabetes. The worsening of their clinical conditions might have led to the introduction of newer drugs and this might have contributed the incidence of prescribing cascade.

Figure 2 depicts the number of prescriptions with prescribing cascade. The data obtained underlines the fact that the adverse drug event as well as its direct influence on prescribing cascade increases with increase in number of drugs. Almost all patients in the study population with more than 10 drugs had prescribing cascade. Hence polypharmacy can be considered as a major risk factor for the development of prescribing cascade.

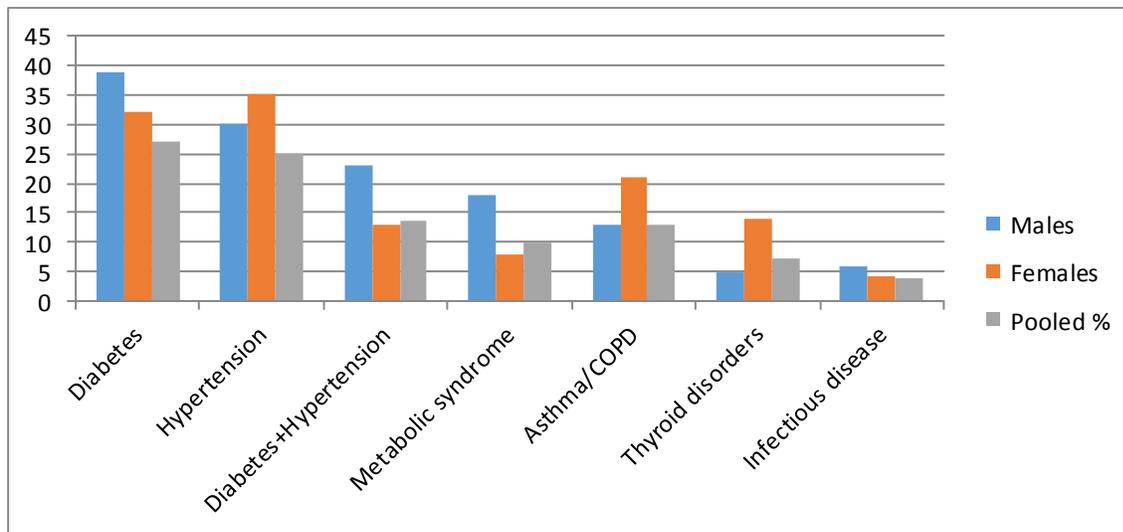


Fig. 1: Medical conditions of the study population

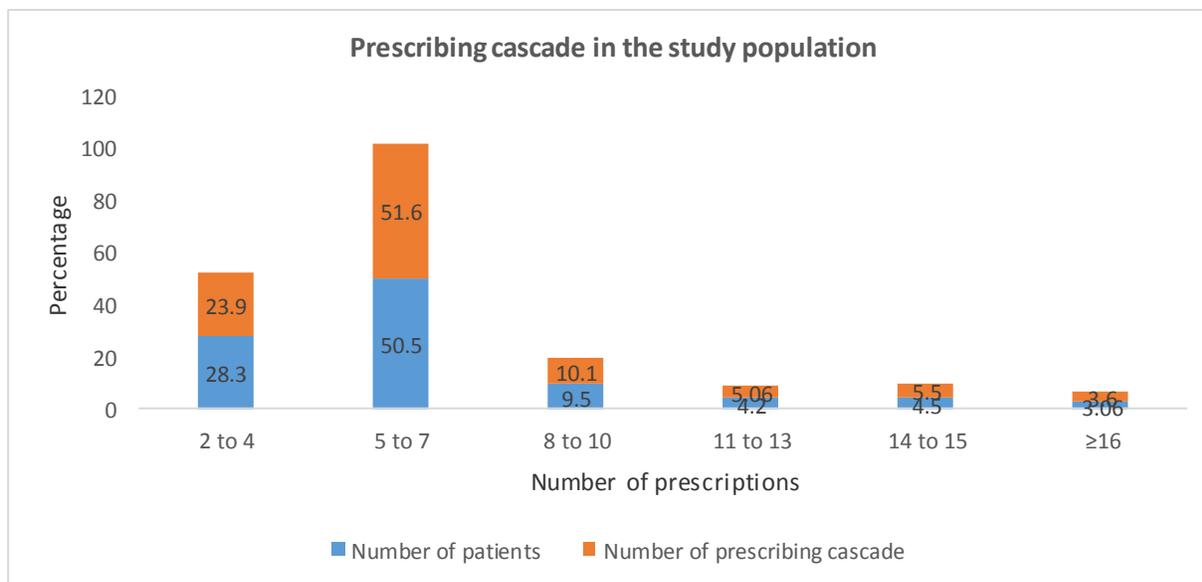


Fig. 2: Prescribing cascade in the study population

### Drugs induced prescribing cascade

On analyzing the prescribing cascade results (Table 3) it is clear that anticipatory prescription in order to prevent the well documented adverse outcomes of some commonly used drugs lead to

the incidence of prescribing cascade. Drugs to correct the electrolyte abnormalities and intolerant side effects like vomiting contributed major share of non-anticipatory prescribing cascade.

**Table 3: List of drugs induced prescribing cascade**

Name of medication	Medication lead new indication/ anticipatory indication	New medication prescribed	No of cases (n=217)	%
Tramadol	vomiting	Antiemetic Ondansetron / domperidone	18	8.2
Furosemide	Hypokalemia	Potassium Chloride supplementation	24	11
Propranolol	Breathlessness	Salbutamol+Ipratropium Nebulization	08	3.6
Calcium Acetate(K.Bind)	Hypomagnesemia	Magnesium supplementation	06	2.7
Olanzapine	Hyperglycemia	Insulin / Oral Hypoglycemic agent	03	1.3
Sucralfate	constipation	Liquid paraffin	07	3.2
Digoxin	Hypokalemia	Potassium Chloride supplementation	04	1.8
Isoniazid	Peripheral neuropathy	Pyridoxine supplementation	02	0.9
Metronidazole	vomiting	Domperidone	05	2.3
Inj.Hydrocortisone	Hyperglycemia	Insulin	08	3.6
Amlodipine	Pedal edema	hydrochlorothiazide	15	6.9
Insulin	Hypoglycemia	Dextrose injection	09	4.1
Aspirin 75 mg	Gastric irritation	Pantoprazole	28	12.9
Phenobarbital	ALP elevation	Ursodeoxycholic acid supplementation	02	0.9
T.Salbutamol	Hypokalemia	Potassium Chloride supplementation	04	1.8
T.Ramipril	Hyperkalemia	Salbutamol nebulization	12	5.5
NSAID	Gastric irritation	PPI/H2 Blocker supplementation	62	28.5

Since the basic reason for prescribing cascade is adverse drug events, risk factors for the development of prescribing cascade remains the same as the risk factors for adverse drug events. Geriatric patients, poly pharmacy prescriptions and patients on 'high risk medicines' including cardiovascular drugs, and anti-infective, are at higher risk of adverse drug events and prescribing cascade as well.<sup>7-9</sup> As the age crosses 65 years, capacity to handle the drug safely in the body decreases. Elderly patients may be at higher risk of prescribing cascades too because of increased chance for misinterpretation of adverse drug reaction to be as the onset of a new medical condition. For example, an extra pyramidal adverse event caused by metoclopramide may be misinterpreted as Parkinson's disease, but this misinterpretation would be less likely in a young people as Parkinson's disease is less prevalent in younger population.<sup>3,6,10</sup>

### CONCLUSION

Retrospective analysis of Polypharmacy prescriptions shows that prevalence of prescribing cascade is high in our population especially in geriatric patients. Since most common adverse drug reactions are dose related, starting therapy with lowest effective doses can prevent development of adverse drug

events to some extent in this population. Patients may not inform their doctor or pharmacist when they experience an adverse drug reaction. Some patients will stop treatment because of an adverse drug reaction without getting advice from their doctor or pharmacist. Many patients will go to another doctor once they suffer from adverse outcome from the treatment and they would not convey the medication history properly to the healthcare provider they visit. So initiation of treatment with lowest effective dose, effective communication and reconciliation of all of the medicines prescribed by the different health professionals caring for a patient is vital to curtail the prescribing cascade.

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