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Monitoring of Adverse Reactions in Geriatric South Indian Patients in a Tertiary Care Teaching Hospital: A Prospective Study.

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ABSTRACT

Physiological variations & Polypharmacy of elderly show more ADR when compare with adult. Hence this study was carried out to see the incidence and type of adverse drug reactions in hospitalized elderly patients in a selected general medicine department. This was a cohort & a cross sectional study, conducted over a period of two years those who satisfy the criteria. Descriptive statistics were applied to the obtained data. Out of 475 cases only 30 have ADR (6.31%). These ADRs were assessed by using a WHO causality assessment scale, Naranjo, Hertwiz scales. WHO scale shows certainly 14 (46.44%), probable or likely 7 (23.33%), possible 9 (30%). Naranjo scale shows Definite 2 (6.6%), possible 1 (3.3%), Probable 27 (90%). Hurwitz's shows 1 (3.3%) severe, mild 4 (13.33%), moderate 25 (83.3%). Interestingly the outcome of the ADR showed improvement as only 3 patients were hospitalized due to ADR while remaining ADRs were observed during the treatment for which alert cards were given for prevention in the future to the patient/care taker. The more common ADR were observed with amlodipine, steroids, amiodarone. Adverse drug reactions are common in all the age groups. So monitoring & prevention of ADR in the elderly is very vital /crucial to prevent the expenses incurred .These studies also showed crave/need for pharmaceutical care in elderly.

Keywords: Adverse drug reactions (ADR); ADR assessment scales; Geriatric; Indian tertiary care.

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INTRODUCTION

According to World Health Organization, adverse drug reaction is defined as, "A response to a drug that is noxious, unintended/untoward effect that occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function", which is in use since 1972. Previous studies reveal that the prevalence of ADRs is more in older populations than adults [1, 2].

As the age advances, many physiological and pathological changes occur in the body which is characterized by the progressive diminished functioning of principle structures such as renal system and hepatic system in the older population. In turn, these are further associated with co-morbid conditions and chronic habits which leads to changes in the pharmacokinetics and pharmacodynamics effects resulting in increased sensitivity of drugs. The outcome is a longer treatment schedule for the patient and in some cases lifelong therapy. This further leads to polypharmacy, which multiplies the risk of ADRs [2, 3, 4]. Among the elderly population, one sixth of hospital admissions are due to adverse drug events [5]. Occurrence of ADRs during hospitalization is more common when compare with the ADR related hospital admissions [6].

Though the use of medications in geriatric patients improves health related quality of life (HRQOL), but side effects accompanied by their use may also lead to overuse/ improper medication adherence. Hence, these aspects need to be considered and the potential benefits against the risks should be weighed while prescribing [3, 7].

The meta-analysis of the observational study showed ADR related hospitalizations among the elderly population were four times higher than in younger population. Development of ADRs in an elderly population increases the morbidity, mortality, hospitalization period, health related costs and even death. The chronic diseases associated co-morbidities and frequent acute exacerbations of diseases places the elderly patients at high risk for ADRs and make identification more challenging [8, 9, 10].

However, the data related to ADRs in India are scarce, especially in elderly patients. There is an extensive demand to find out the data regarding the occurrence, nature, causative drugs, severity, risk factors for the development of ADRs and preventable measures [3].

Hence, the present study was performed to analyze the incidence, pattern, type of ADRs, and outcome of the most commonly causing drugs in elderly hospitalized patients.

METHODOLOGY

The elderly patients who satisfy the inclusion criteria were included in this study after obtained the ethical clearance by taking their consent. The Patients of either sex of 60 years and above willing to give informed consent form of Selected chronic disease patients ((Hypertension, Heart failure, IHD, Hyperlipidaemia, Osteoporosis, Arthritis, Diabetes Mellitus, COPD, Cerebrovascular disease, Chronic pancreatitis, Acid peptic ulcer disease)included. The exclusion criteria was who are in a coma/mechanically ventilated for long time (>3months). This study was conducted from June 2012 – June 2014 in the selected general medicine departments. The enrolled patient's treatment pattern was observed for the day of admission to discharge. The ADRs observed patients were informed about their ADR & even to their caretaker for further prevention of Adverse drug reaction and its related expenses by providing alert cards. The various scales were used for assessing the observed ADR and the obtained data was subjected for descriptive statistics (i.e. Percentage)

RESULTS

Out of 475 patients, ADRs was observed in 30 patients (6.3%), of which majority were in the age group of 60-65years (11; 36.7%), followed by age group of 66-70 years (8; 26.7%), 71-75 years (7; 2.3%), 76-80 years (2; 6.7), 81-85 years (1; 3.3%) and 90-96 years (1; 3.3%) age group. Out of 30 ADRs, 20 (66.67%) were developed in males and 10 (33.33%) were in females. The Incidence of ADRs was 7.43% and 4.8% among men and women respectively in the total study population (Fig. 1).

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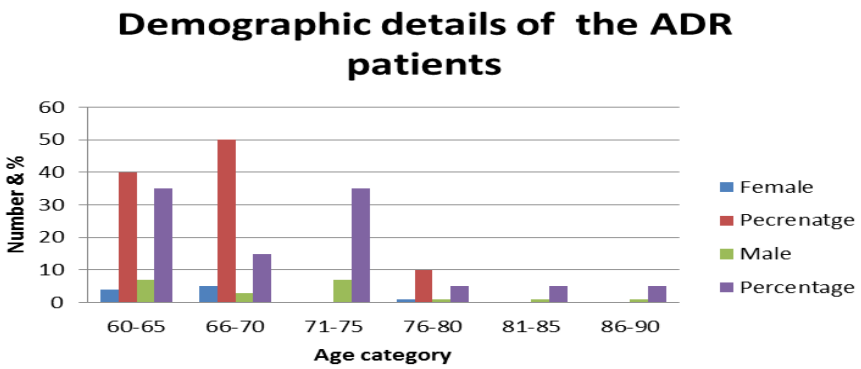

Figure 1: Demographic details of the patients

The Majority of reported adverse drug reactions had affected endocrine system (8; 26.7%) followed by renal system (7; 23.33%), general effects (7; 23.33%), gastrointestinal system (3; 10%). The least affected systems were eye, skin, renal, hepatic and nervous systems (one ADR in each).

Table 1: System wise Distribution of ADRs Occurred in Elderly

System affected	Effect	Frequency
Endocrinology	Hypothyroidism	3
	Steroid induced DM	3
	Steroid induced Cushing's syndrome	1
	SIADH	1
Renal System	Pedal edema	3
	Edema	1
	AKI	1
	Ankle edema	1
	Hematuria	1
General	Hyponatremia	2
	Hyperkalemia	2
	Hypersensitivity reaction	3
GIT	GI Bleed	2
	Hiatus hernia and GI changes	1
Respiratory system	ILD	1
Skin	SJS	1
Nervous System	Stiffness, tremor, rigidity	1
Hepatic system	ATT induced Hepatitis	1
Eye	Steroidal induced Glaucoma	1

Cardiovascular agents are the drugs most commonly causing ADRs followed by steroids, antibiotics, drugs acting on the nervous system and anti- tubercular drugs (Table 1).

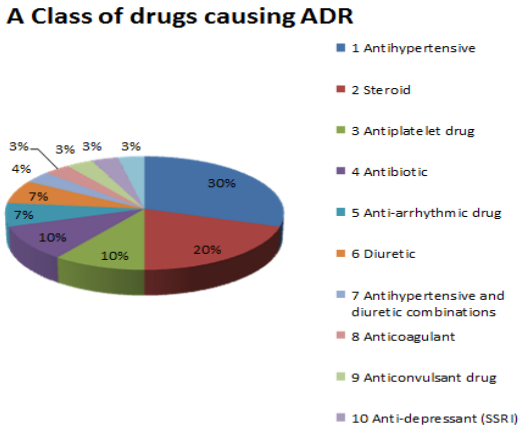

Figure 2: A class of drugs involved in causing of ADRs

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Type C (chemical; 60%) ADRs accounted the major fraction of ADRs developed in the study population. Table 2 shows the classification of observed ADRs according to Williams and Brown.

Table 2: Classification of ADRs based on Williams & Brown (General)

S. No.	ADR classification	Number & %
1	Type A - Augmented	7(23.3)
2	Type B - Bizarre	0
3	Type C - Chemical/Chronic	18(60)
4	Type D - Delayed	2 (6.7)
5	Type E - Exit/end of use/Withdrawal	0
6	Type F - Familial	0
7	Type G - Genetic	0
8	Type H - Hypersensitivity	3 (10)
9	Type U - Unclassified	0
	Total	30

The causality assessment of the ADRs was steered by using both the WHO – UMC criteria Naranjo's scale and **Hartwig scale**. The causality assessment by WHO – UMC scale results showed that, the majority of cases belongs to certain (14; 46.7%) followed by possible (9; 30%) and probable or likely (7; 23.3%). No cases fell into the category of unlikely or doubtful and conditional or unclassifiable as shown in the Figure 3.

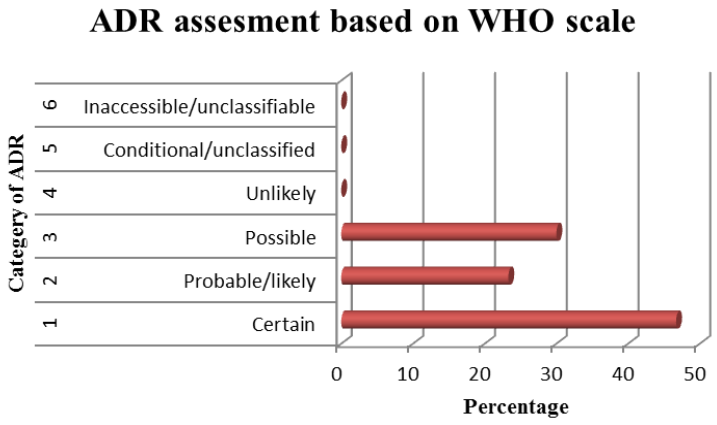

Figure 3: ADR assessment based on WHO scale

Causality assessment done by Naranjo ADR probability scale showed majorly probable (27; 90%) followed by definite (2; 6.6%) and possible (1; 3.4%) ADRs. No doubtful ADRs were developed in the study population (Figure 4).

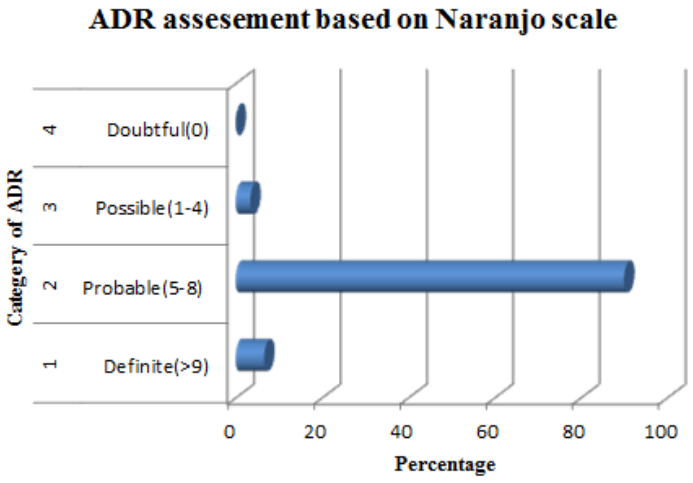

Figure 4: ADR assessment based on Naranjo scale

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Hartwig scale Severity assessment results showed, out of 30 adverse drug reactions, 25 (83 %) were moderate, 4 (14%) were mild severe and 1 (3%) was severe in nature (Figure 5).

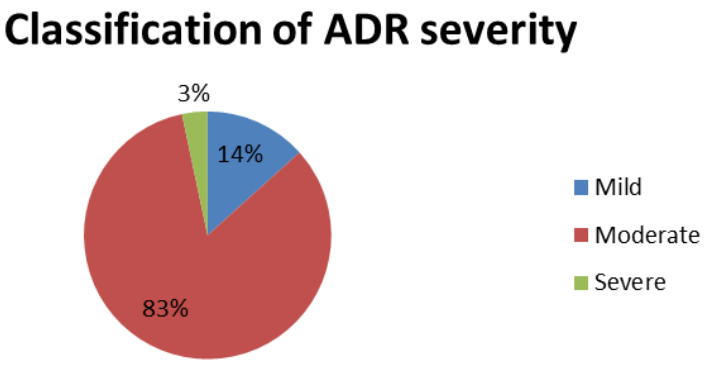

Figure 5: ADR assessment based on Hart wig scale (Severity)

Interestingly, all the ADRs outcome or management showed an improvement. Except one which was discharged in half of the course of the therapy or management due to financial constraint.

Table 3: Types of ADR (with ATC Code) in Female patients

S. No.	Drug involved	ATC code	ADR effect
1	Prednisolone	S01BA04	Glaucoma
2	ATT Kit		Hepatitis
3	Telmisartan	C09CA07	Hyponatremia
4	ARB & spironolactone	C03DA01	Hyperkalemia
5	Amiodarone	C01BD01	Hypothyroidism
6	Phenobarbitone	N03AA02	SJS
7	Penicillin	J01CA01, J01CF02	Allergy (Hypersensitivity reaction)
8	Escitalopram	N06AB10	Induced SIADH
9	Estrogen chemotherapy Drug (HRCT)	H02AB06	ILD (interstitial lung disease)
10	Steroid (Prednisolone)	H02AB06	Induced DM

Table 4: Types of ADRs (with ATC Code) in Male patients

S. No.	Drug involved	ATC code	ADR outcome
1	Enlapril	C09AA02	pedal edema
2	cefuroxime, cefazolin	J01DC02	Hypersensitive reactions
3	Aldosterone (spironolactone)	C03DA01	Hyperkalemia
4	Reserpine		Stiffness, tremor, rigidity
5	Amiodarone	C01BD01	Hypothyroidism
6	Amiodarone	C01BD01	Hypothyroidism
7	amlodipine	C01BD01	Ankle edema
8	Amlodipine	C01BD01	Edema
9	ARB (Telmisartan 2.5 mg,)	C09CA07	AKI
10	Steroid(Prednisolone)	H02AB06	DM
11	Amlodipine	C01BD01	Pedal edema
12	Penicillin's – Ampicillin and amoxicillin	J01CA01, J01CF02	Allergy (hypersensitive)
13	Amlodipine (T. Amlodac)	C01BD01	Pedal edema
14	Hydrochlorothiazide	C03AA03	Hyponatremia
15	Aspirin	B01AC06	GI Bleed
16	Wysolone(Prednisolone)	H02AB06	DM
17	Steroid (Prednisolone)	H02AB06	Cushing's syndrome
18	Aspirin	B01AC06	GI Bleed
19	Antiplatelet/anti-coagulant (warfarin)	B01AA03	Hematuria
20	Aspirin	B01AC06	Hiatus hernia ,GI changes

DISCUSSION

Adverse drug reactions generally cause morbidity and mortality. Hence, the awareness on ADRs is important to the physicians to prevent certain life threatening situations. ADRs were the fourth leading cause

of death in USA [3]. In recent years, monitoring, documenting and reporting of ADRs have got a lot of importance all over the world. In India, pharmacovigilance program has been started since 2005, even though the activities carried out are much less when compared to our western counterparts. The major reason for poor reporting of ADRs is mainly the lack of awareness among health care workers and even the patient population. This clearly suggests the need of strengthening this area to increase the reporting and build a meaningful directory which can help the population.

The elderly are most susceptible to development of ADRs among various patient populations. Numerous confounding factors include multiple disease, polypharmacy, genetic, ethnic, dietary, environmental, etc. Hence, continuous monitoring of ADRs of the prescribed medication is an essential aspect of therapeutics. Due to lack of awareness and the busy schedule of the physicians, ADRs are often un-reported. Health-related accreditation bodies estimate that 95% of all ADRs are not reported [20]. The pharmacist can play a pivotal role in this area and help prevent ADR associated issues, especially in elderly by complimenting the physicians in therapeutic management of the disease.

In our study, we found that 30 out of 475 geriatric patients (6.3%) developed ADRs which is comparable to the reported incidence of ADRs of 3-6% in the general population [11] and whereas, it is lesser than that found in a study conducted by Davies EC et al. in geriatric patients from the UK (14.7) [12] and from USA and Europe (20%) [13]. This clearly suggests that there is a need for more departmental cooperation and focus in this research area.

It was identified that cardiovascular agents are the drugs most commonly causing ADRs followed by steroids, antibiotics. The findings was in line with similarly conducted and reported studies which showed antibiotics, cardiovascular drugs (anticoagulants, digoxin, diuretics) hypoglycemic agents, antineoplastic agents and nonsteroidal anti-inflammatory drugs (NSAIDs) as drugs responsible for increased incidence of hospitalization or causing ADRs during hospitalization [13].

A majority of ADRs developed among males (66.67%) which are similar to a study conducted by Sivanandy Palanisamy [10] (56.67%) and in contrast to studies carried out by Klein U and Hallas J et al. [14,15]. However, there are a few studies that do not show any association between occurrence of ADRs and gender. [16]. The prevalence of endocrine system ADRs is high followed by renal system, whereas in the study carried out by Rima Shah et al [3, 17, 18] a high prevalence in the gastro intestinal followed by cardiovascular and endocrine system was observed.

In general, among elderly patients, majority of ADRs observed are type A (dose related augmented) but in our study, we found that the majority were caused by type C (18; 60%) followed by type A (7; 23.3%) [19]. Hence, geriatric clinical pharmacology will continue to be an important area of research, which should be continuously studied.

CONCLUSION

This study suggests that ADR monitoring and preventions are very essential in elderly for preventing long term hospitalization and higher treatment costs. This study also showed the dearth of experts for providing pharmaceutical care services to geriatric population. The current study was done in a small pool of patients from different regions for a short duration of 2 years. A larger selection of geriatric patients for a longer duration to assess the socio-economic impact throughout India. Future studies involved in pharmaco-genomics and continuing pharmaco-vigilance in the elderly are the need of the hour.

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