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A Cross-Sectional Study to Evaluate the NSAID's usage among Elderly Patients Admitted to Medicine & Orthopaedic Wards at a Teaching Hospital: Insight into Prescription Pattern & Adverse Drug Reactions

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ABSTRACT

Introduction: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are indicated in the treatment of various inflammatory conditions and also concomitant with antimicrobial agents. Recent studies have shown that NSAIDs are most commonly prescribed in orthopaedics and medicine wards in hospitals. NSAIDs demonstrate various adverse reactions which reduce the quality of patients' life. Recent studies have reflected that NSAIDs are associated with increased risk of hospitalization and death from gastrointestinal bleeding and perforation.

Aim: The main aim of the present study was to evaluate the NSAIDs usage with an insight into WHO recommended standards on prescribing indicators, use of essential medicines & Adverse Drug Reactions among elderly patients.

Methodology: The present short-term research study was conducted amongst the elderly patients (above 65 years of age) (*n=50*) retrospectively for duration of two months. Patients' case record files from Medical Record Department were evaluated from Medicine & Orthopaedics ward. The details such as duration of hospital stay, total number of medicines prescribed, name of the drug and group of medicines, route of administration, use of generic names in prescription, and also total number of drugs prescribed in each patient were evaluated. Case records were analyzed having prescription with more than two medicines prescribed including at least one analgesic drug (NSAIDs). We studied their prescription pattern, use of essential medicines & Adverse Drug Reactions and laboratory investigations.

Results and Conclusion: The present study assessed the tendency of clinician to prescribe by generic name, International Non-proprietary Names (INNs) of drugs based on WHO recommended standards on prescribing indicators. The prescribing pattern showed that out of 50 prescriptions studied (n=50), generic names were prescribed in 8% while brand names were prescribed in 92% of prescriptions. The fixed dose combinations (FDCs) were found to be 34%, among which Acetaminophen + Diclofenac, Aspirin + Clopidogrel and Aspirin + Atorvastatin were mainly prescribed. It was reported that 64% had oral route, 6% parenteral and 30% both oral and parenteral routes of administration in prescriptions. Adverse drug events of gastric reflux and acidity were found in 10% of cases. We also studied the lab investigations, prothrombin time, bilirubin, creatinine and LDH were reported to be higher in 22%, 6%, 16% and 10% cases respectively; serum urea was higher in 22% while lower in 6% cases; SGOT was higher in 4% cases while lower in 6% cases & SGPT was higher in 4% cases. Rise in prothrombin time, urea, creatinine, SGOT, SGPT, bilirubin is seen with longer use of NSAIDs along with other drugs, suggesting influence of NSAIDs on hematologic, liver and renal profile. Thus, only judicious concurrent use of NSAIDs & other multiple drugs should be promoted keeping mind the health, financial and comorbidity related factors in elderly patients.

Key words: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), Prescribing Pattern, Geriatric, Adverse Drug Reactions, Essential Medicines, Fixed-Dose Combinations

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly prescribed classes of drugs globally, accounting for approximately 5-10% of all medications prescribed each year as reported by various researchers. It has been documented that NSAIDs show various side effects which reduce the quality of patients' life, interfere with drug compliance, and cause inadequate management [1, 2]. Besides used as analgesics and antipyretics till date, NSAIDs are to a great extent indicated for the pharmacotherapy of rheumatological disorders, in orthopaedics & medicine outpatients and inpatients admitted in hospitals. Earlier research studies [6, 7, 8] have shown that the proportion of Geriatric age group, the most common group to be admitted in hospitals, has been constantly increasing over the last few years as they have

at least one chronic disease and suffer from various conditions [6, 7, 8]. NSAIDs share a common mechanism of action of inhibition of prostaglandin synthesis & produce their pharmacological actions such as antipyretic, analgesic, and anti-inflammatory activities [2]. Recent studies have reflected that NSAIDs are associated with increased risk of hospitalization and death from gastrointestinal bleeding and perforation [3, 4]. Analgesics are commonly used inappropriately among elderly age group patients. Taking several drugs, in particular, has been linked to higher health-care expenses as well as an increased risk of adverse drug events (ADEs), drug interactions, medication non-adherence, impaired functional ability, and various geriatric syndromes [9]. It is reflected from the recent studies that NSAIDs are associated with increased risk of hospitalization and death from gastrointestinal bleeding and perforation [3, 4], as they are commonly indicated inappropriately among elderly persons. Taking several drugs, in particular, has been linked to higher healthcare expenses as well as an increased risk of Adverse Drug Events (ADEs), drug interactions, medication non-adherence, impaired functional ability, and various geriatric syndromes [9]. Researchers [10] have concluded that using chronic NSAIDs without prophylactic gastro-protective agents, self-medication, polypharmacy and drug-drug interactions were the main problems identified. While prescribing NSAIDS in elderly, it is given along with multiple other drugs. This increases Fixed DoseCombinations (FDC), polypharmacy and increased AdverseDrug Events (ADEs) [9,10].

Adverse drug reactions (ADRs) are an important public health problem, representing a major cause of morbidity and mortality. Adverse drug reactions (ADR) are common occurrences in a hospital setting. An adverse drug reaction (ADR) is defined as a noxious, unintended injury that arise from drug related causes. The growing evidence on the increased frequency and severity of ADRs, associated with a negative impact on patient's health status, also reveals that ADRs entail a significant burden on healthcare facilities, increasing the length of hospital stay, and requiring sometimes additional investigations and drug therapies for the treatment of symptoms and diseases caused to the patient [10-12].

Fixed-Dose Combination (FDCs) [13-16] are medicines which contain two or more active ingredients in fixed proportions in the same formulation, also called as "Fixed Ratio Combinations". Recently, the formulation in fixed-dose combinations and clinical development studies are increased for their use in treating various diseases [17]. Evaluation of drug utilization patterns needs to be done frequently to enable suitable amendments in the prescription of drugs to increase the therapeutic benefit and decrease the adverse effects. Hence, prescribing pattern studies are conducted to monitor, evaluate and if necessary, suggest modifications in the prescribing behavior of healthcare professionals to ensure rational and

cost-effective healthcare [17-19]. Rational Use of Medicines (RUM) is an issue that has global importance, as it aims at evaluating the accessibility, availability, and correct prescribing of the drugs [19]. As quoted by World Health Organization (WHO) [20, 21] which states that irrational prescribing is a global issue. As per WHO the Rational Use of Medicines (RUM) is "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" [20, 21]. It is recommended by WHO to monitor ADRs and develop a well-established pharmacovigilance system [22]. The pharmacovigilance programme of India which is running across the country also stresses on rational and watchful use of medicine to ensure safe and effective use of medicines and avert the negative sequel of pharmacotherapy [22].
Essential medicines [23] are those that satisfy the priority health care needs of the population. They are selected to ensure the efficacy and safety of patients. Essential medicines are intended to be available within the context of functioning healthcare systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility [23, 24, 25].

MATERIALS AND METHOD

The present short-term study (STS) of duration of two months was designed as a retrospective observational study type. The study was initiated after approval from the Sumandeep Vidyapeeth Institutional Ethics Committee (SVIEC). The research work was carried out retrospectively in 50 elderly patients (n=50) age more than 65 years, who were prescribed atleast one of the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). The necessary data from patient case files was retrieved from the medical records department of Medicine & Orthopaedic wards of Dhiraj Hospital, a rural teaching tertiary care hospital, attached to Smt. B. K. Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth an Institution deemed to be University, Piparia, Vadodara, Gujarat. Collected details were used for scientific purpose only and identification of patient was not disclosed. Also, the diagnosis, relevant medical history, data from prescriptions and lab investigations were recorded in excel sheet and presented in form of percentages in results.

Data were statistically analysed by using appropriate analytical tests like chi-square test, t test, or percentile. P values considered to be significant if less than or equal to 0.05 ($p \leq 0.05$).

RESULTS

The present research study was retrospective observational type. Total 50 number of patients (*n=50*) were recruited based on the methodology and selection criteria. As the study was of retrospective type, patients' case record files *(n=50)* from medicine and orthopedic wards were collected during last one year. The data included were of elderly patients who were prescribed at least one of the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).

As depicted in Table 1a-1d/Figure 1a-1b, demonstrates the total duration of hospital stay amongst the elderly patients. It was reported that, nearly 54% were hospitalized for less than 6 days followed in decreasing percentage from 6 to 10, 10 to 20 and more than 20 [Table 1a-1d/Figure 1a-1b].

Table 1a: Total number of days of Hospital stay of elderly patients

Total duration of Hospital Stay (no. of days)	**Number of patients (n=50)**	**Percentage (%)**

Less than 6 days	17	54%
6 to 10 days	10	20%
10 to 20 days	9	18%
More than 20 days	4	8%

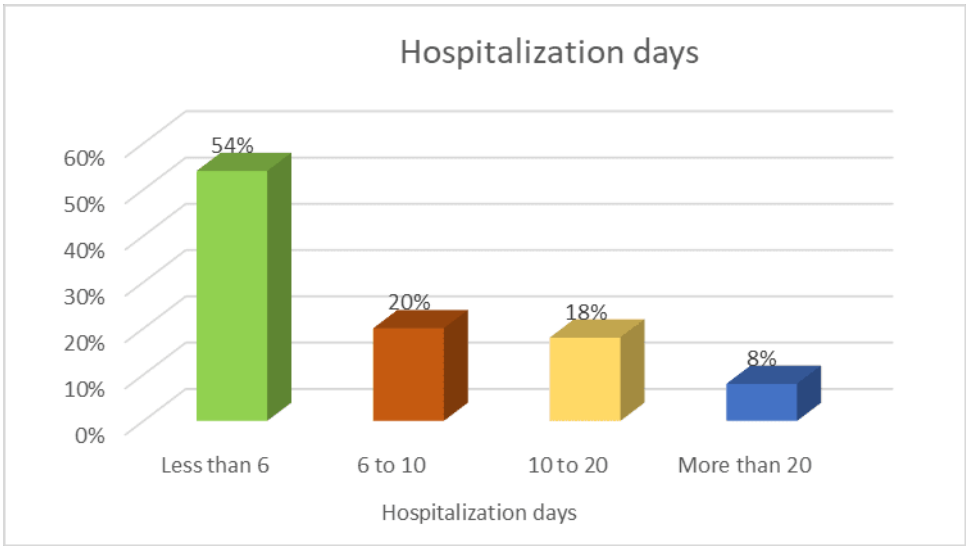

Figure 1a: Total number of days of Hospital stay of elderly patients

Table 1b: Number of days of hospitalization among patients with and without polypharmacy

Number of days of hospitalization	WITH POLYPHARMACY (At least 5 drugs) (n=43)	Percentage with polypharmacy (%)	WITHOUT POLYPHARMACY (less than 5 drugs) (n=7)	Percentage without polypharmacy (%)
Less than 6 days	20	46.51%	7	100%
6 to 10 days	10	23.25%	0	
10 to 20 days	9	20.93%	0	
More than 20 days	4	9.30%	0	

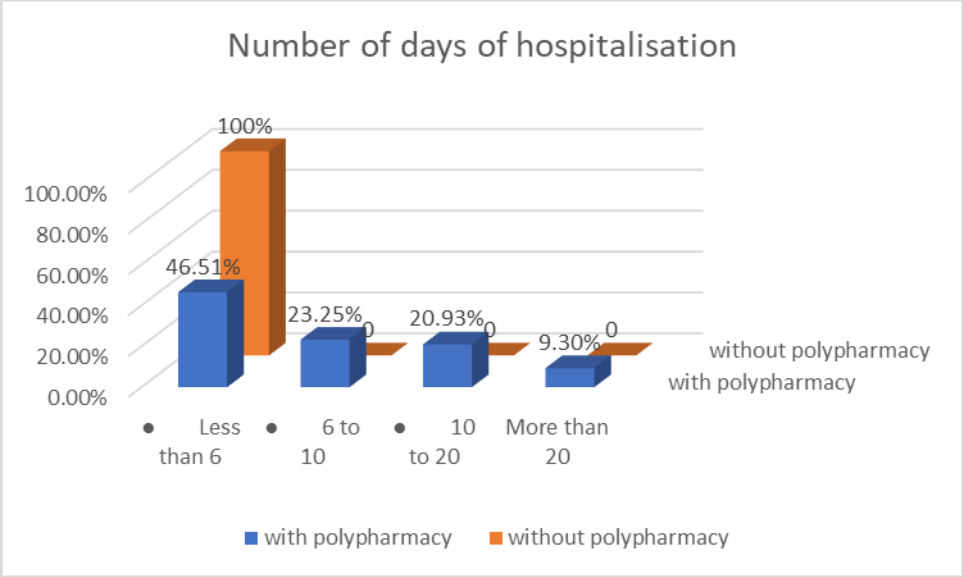

Figure 1b: Number of days of hospitalization among patients with and without polypharmacy

Table 1c: Gender wise duration of number of days of hospital stay

Gender wise duration of hospital stay	Males (n=26)	Percentage males (%)	Females (n=24)	Percentage Females (%)
Number of days of hospitalization				
Less than 6 days	16	61.53%	11	45.83%
6 to 10 days	3	11.53%	7	29.16%
10 to 20 days	4	15.38%	5	20.83%
More than 20 days	3	11.53%	1	4.16%

Table 1d: Geriatric age-group distribution of duration of hospital stay

Geriatric age-group distribution of duration of hospital stay	Age 65-69 years (n=25)	Percentage 65-69 yrs (%)	Age 70-74 years (n=11)	Percentage 70-74yrs (%)	Age 75-79 years (n=10)	Percentage 75-79yrs	Age 80-84 years (n=4)	Percentage 80-84 yrs (%)

						(%)		
Less than 6 days	14	56%	7	63.63%	3	30%	2	50%
6 to 10 days	5	20%	1	9.09%	3	30%	2	50%
10 to 20 days	4	16%	2	18.18%	3	30%	0	0
More than 20 days	2	8%	1	9.09%	1	10%	0	0

We studied the prescribing pattern, wherein those prescriptions having fixed dose combinations (FDCs) where 17 number (17 FDC) amongst the elderly patients; were noted to be 34% amongst 50 prescriptions (n=50).

Mainly Diclofenac + Acetaminophen was used followed by Aspirin + Atorvastatin, Aspirin + Clopidogrel, Aspirin + Rosuvastatin, Telmisartan + Chlorthalidone, Levodopa + Carbidopa was used only once [Table 2a, 2b,2c/Figure 2a,2b].

Table 2a: Evaluation of Fixed Dose Combinations (FDCs) in prescription

Evaluation of fixed dose combinations in prescription	**Number of patients (n=50)**	**Percentage (%)**
Total number of prescriptions with FDC	**17 number of prescriptions with FDC**	**Total = 34%**
Diclofenac + Acetaminophen Out of 17 prescriptions	8	47.06%
Aspirin + Clopidogrel Out of 17 prescriptions	3	17.65%
Aspirin + Atorvastatin Out of 17 prescriptions	3	17.65%
Aspirin + Rosuvastatin Out of 17 prescriptions	1	5.88%

Telmisartan + Chlorthalidone Out of 17 prescriptions	1	5.88%
Levodopa+Carbidopa out of 17	1	5.88%

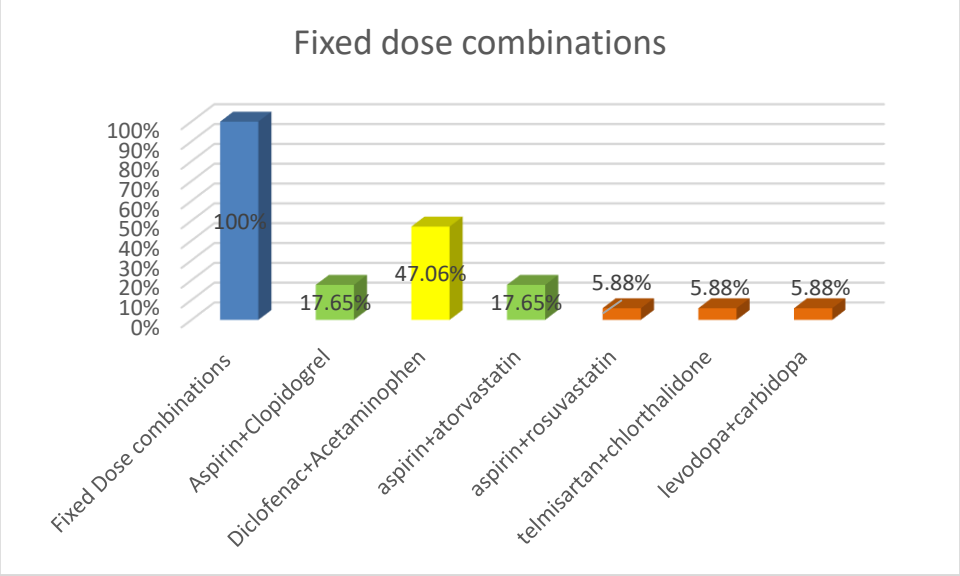

Figure 2a: Details of fixed dose combinations (FDCs) in prescription writing

Table 2b: Gender wise distribution of Fixed Dose Combinations (FDCs)

Gender wise distribution of fixed dose combinations	Males (n=26)	Percentage males (%)	Females (n=24)	Percentage Females (%)
Fixed dose combinations				
Present	9	34.61%	8	33.33%
Absent	17	65.38%	16	66.67%

Table 2c: Geriatric age-group distribution of Fixed Dose Combinations (FDCs)

Geriatric age-group distribution	Age 65-69 years	Percentage 65-69 yrs	Age 70-74 years	Percent age 70-	Age 75-79 years	Perc enta	Age 80-84 years	Percenta ge 80-84

of Fixed Dose Combinations	(n=25)	(%)	(n=11)	74yrs (%)	(n=10)	ge 75-79yrs (%)	(n=4)	yrs (%)
FDCs								
Present	8	32%	4	36.37%	3	30%	2	50%
Absent	17	68%	7	63.63%	7	70%	2	50%

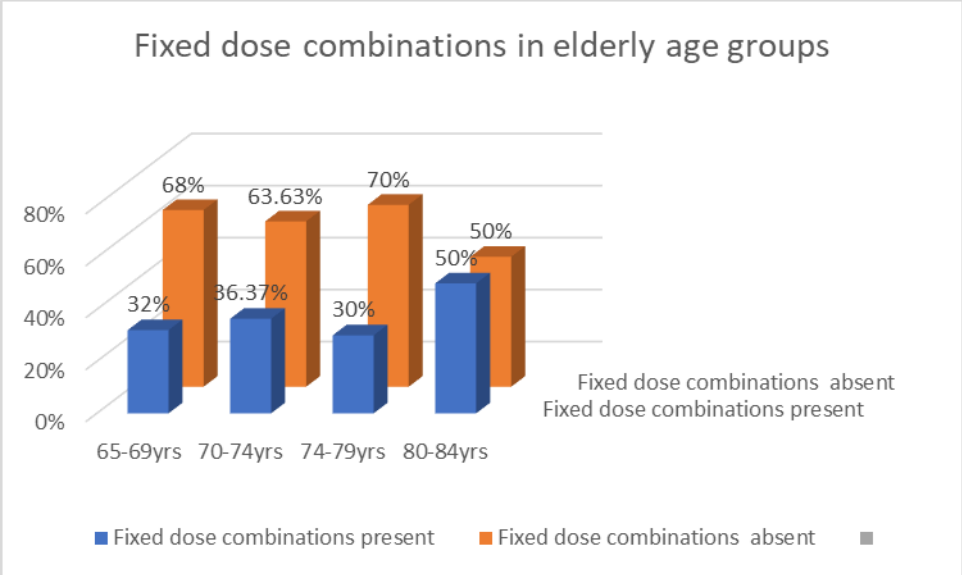

Figure 2b: Fixed dose combinations (FDCs) in elderly age groups

Adverse drug events were also studied as shown in Table 3a – 3e/ Figure 3a-3c which were found in 10% of cases from the patients' case files as depicted in [Table 3a – 3e/ Figure 3a-3c], which included gastric reflux and acidity.

Table 3a: Adverse Drug Events (ADEs) reported

Adverse drug events in study population	Number of patients (n=50)	Percentage (%)
Adverse drug events	**5**	**10 %**

Table 3b: Adverse drug events in patients with and without polypharmacy

Adverse drug events in patients with and without polypharmacy	WITH POLYPHARMACY	Percentage with polypharm	WITHOUT POLYPHARMACY	Percentage without polypharma

	(At least 5 drugs) (n=43)	acy (%)	(less than 5 drugs) (n=7)	cy (%)
Cases of adverse drug events	5	11.62%	0	0

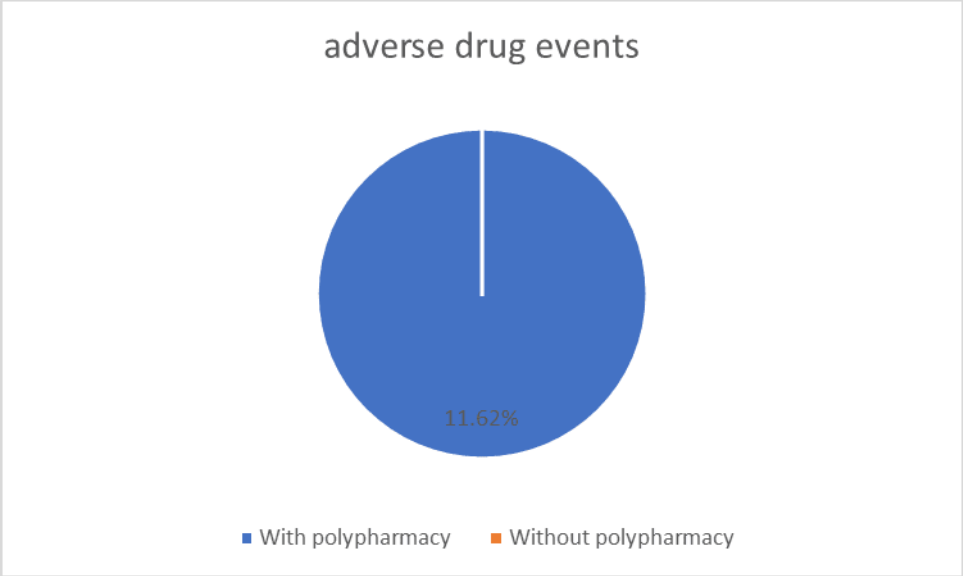

Figure 3a: Adverse drug events in patients with and without polypharmacy

Table 3c: Gender wise distribution of adverse drug events

Gender wise distribution of adverse drug events	Total number of patients n=50	Males (n=26)	Percentage males (%)	Females (n=24)	Percentage Females (%)
Adverse drug events	50	2	7.69 %	3	12.50 %

Table 3d: Geriatric age-group distribution of adverse drug events

Geriatric age-group	Age	Percent	Age 70-	Percent	Age	Perc	Age 80-	Percenta

distribution of adverse drug events	65-69 years (n=25)	age 65-69 yrs (%)	74 years (n=11)	age 70-74yrs (%)	75-79 years (n=10)	entage 75-79yrs (%)	84 years (n=4)	ge 80-84 yrs (%)
Adverse drug events	2	8%	1	9.09%	0	0	2	50%

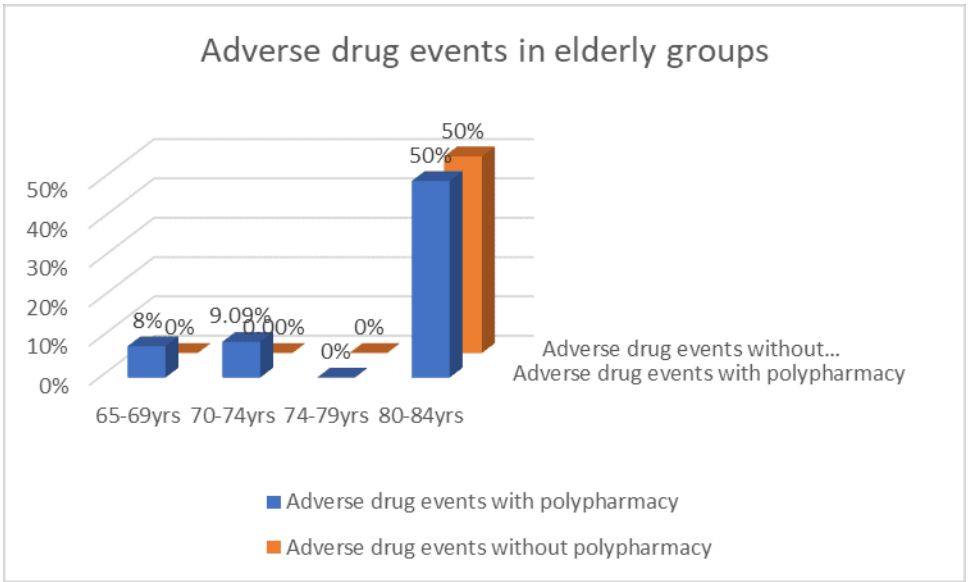

Figure 3b: Geriatric distribution of adverse drug events

Table 3e: Adverse drug events in prescriptions containing enlisted NSAIDs group of drug

NSAIDs group of drugs	Adverse drug events in prescription containing NSAIDs
Aspirin 75 mg tablet	40%
Paracetamol tablet	20%
Paracetamol IV	20%
Diclofenac and Paracetamol	20%
More than one NSAIDs	100%

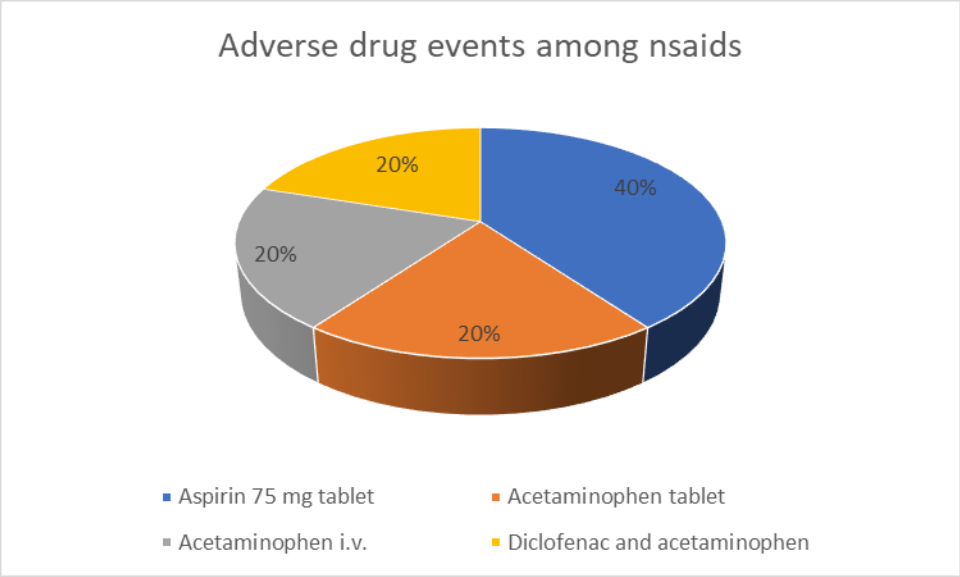

Figure 3c: Adverse drug events in prescriptions containing enlisted NSAIDs group of drug

Laboratory investigations from the patients' case record files were evaluated. The levels of following laboratory investigation parameters were recorded [Table 4a-4c & Figure 4a to 4h].

Table 4a: Laboratory Investigations - Hematology and Urine Analysis

Hematology	Percentage of patients higher than normal range value (n=50)	Percentage of patients lower than normal range value (n=50)	Percentage of within normal range value (n=50)

Hb level in Men: 13.5-17.5 women: 12.0 -15.5 mg/dL	2	56	32
Total Count	18	0	82
Neutrophils	52	6	42
Lymphocytes	2	38	60
ESR	34	-	66
Platelets	12	0	88
Prothrombin time	22	0	78
URINE			
Albumin	10	-	90
Sugar	2	-	98

Table 4b: Glucose, Renal and Hepatic Lab Investigations

SUGAR	**Percentage of patients**	**Percentage of patients lower than normal**	**Percentage of patients within normal range**
RBS	8	2	90
FBS	4	0	96
PP2BS	0	0	100

RENAL			
Na	2	0	98
K	0	4	96
Cl	0	4	96
Urea	22	6	72
Creatinine	16	0	-
HEPATIC			
Total protein	-	8	-
Albumin	-	10	-
Globulin	-	2	-
Bilirubin	6	-	-
SGOT(AST)	4	6	-
SGPT(ALT)	4	-	-

Table 4c: Cardiac lab investigations

CARDIAC	Percentage of patients higher thannormal (n=50)	Percentage of patients lowerthannormal (n=50)	Percentage of patients withinnormalrange (n=50)
LDH1	10	-	-
CRP	20	-	-

Among the mentioned lab parameters, following were the main parameters that were reported to be affected by pharmacodynamics of NSAIDs along with other drugs. The clotting time increased in 22% cases as prothrombin time is shown to increase on use of NSAIDs. [Table 4a/Figure 4b].

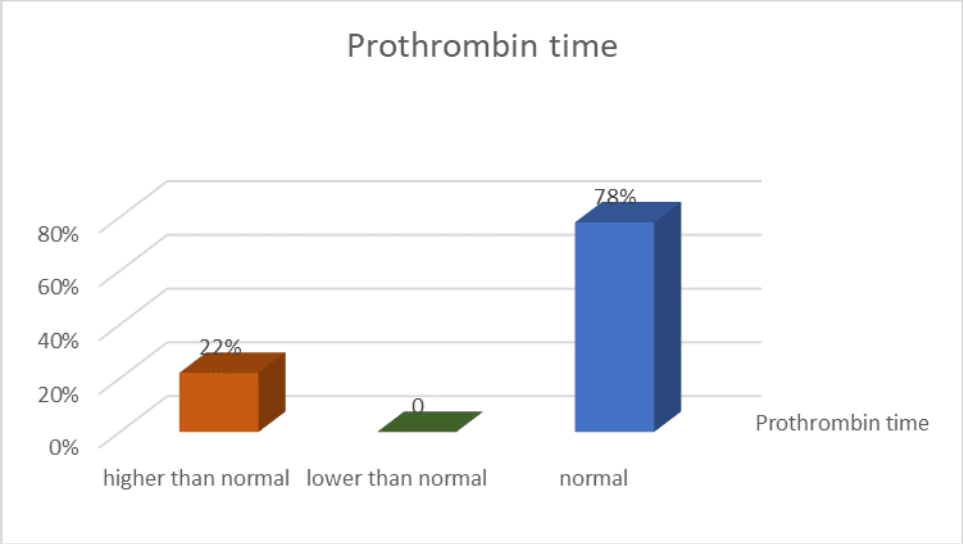

Figure 4a: Prothrombin time

In renal tests, urea increased in 22% and decreased in 6% cases. [Table 4b/Figure 4b, 4c] while creatinine increases in 16% cases.

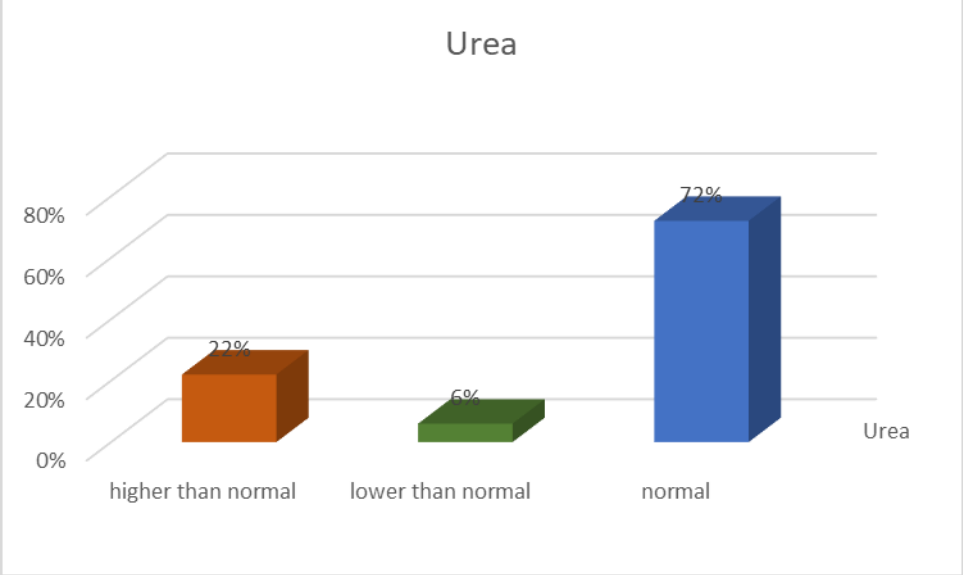

Figure 4b: Urea

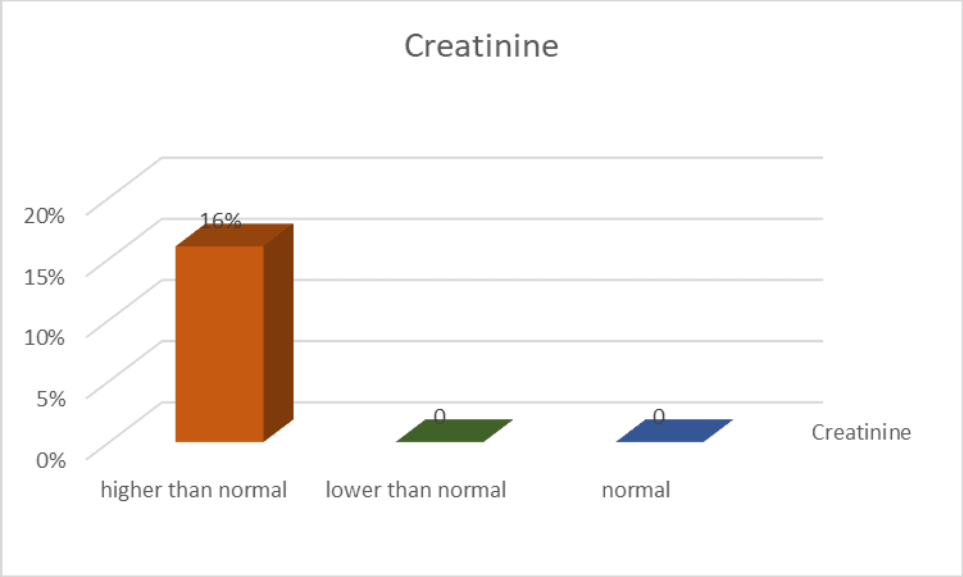

Figure 4c: Creatinine

Liver function tests depicted in Table 4b and Figure 4d-4e showed increased bilirubin levels in 6% cases,4% have increased SGOT while 6% have decreased SGOT, 4% of them have increased SGPT levels (n=50).

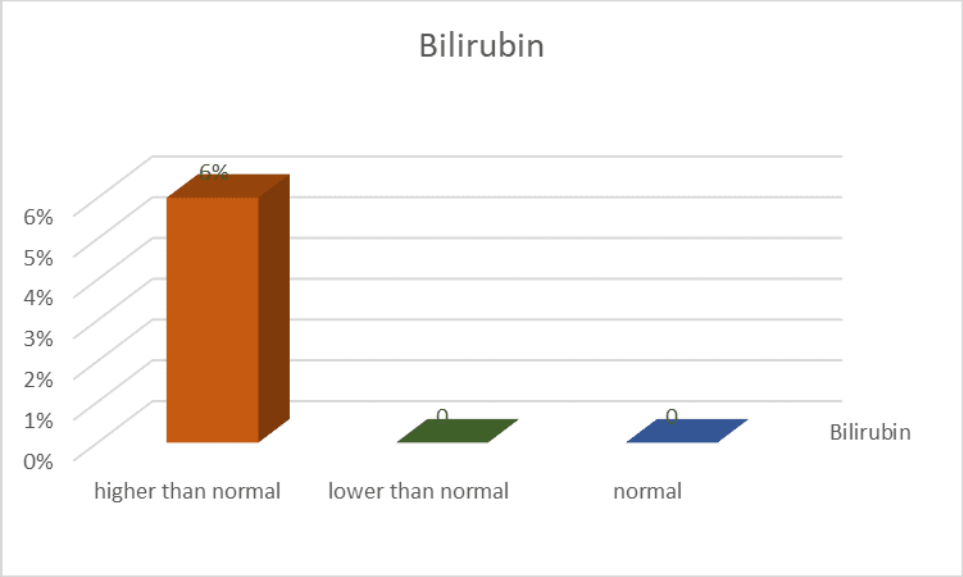

Figure 4d: Bilirubin

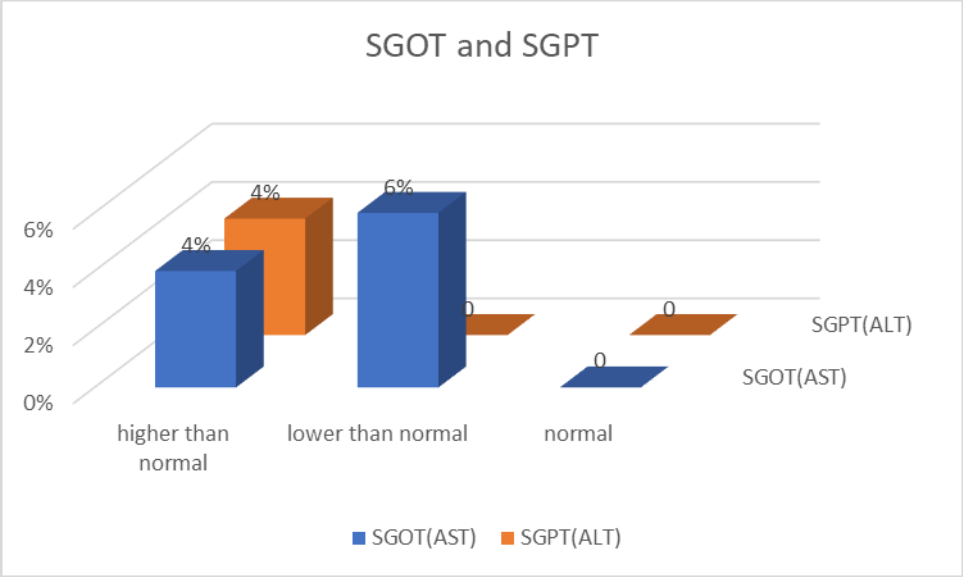

Figure 4e: SGOT and SGPT

In tests related to cardiac functions, 10% were found to have increased LDH1 levels. [Table 4c/ Figure 4f] and 20% increased C-reactive proteins [Table 4d/Figure 4g]

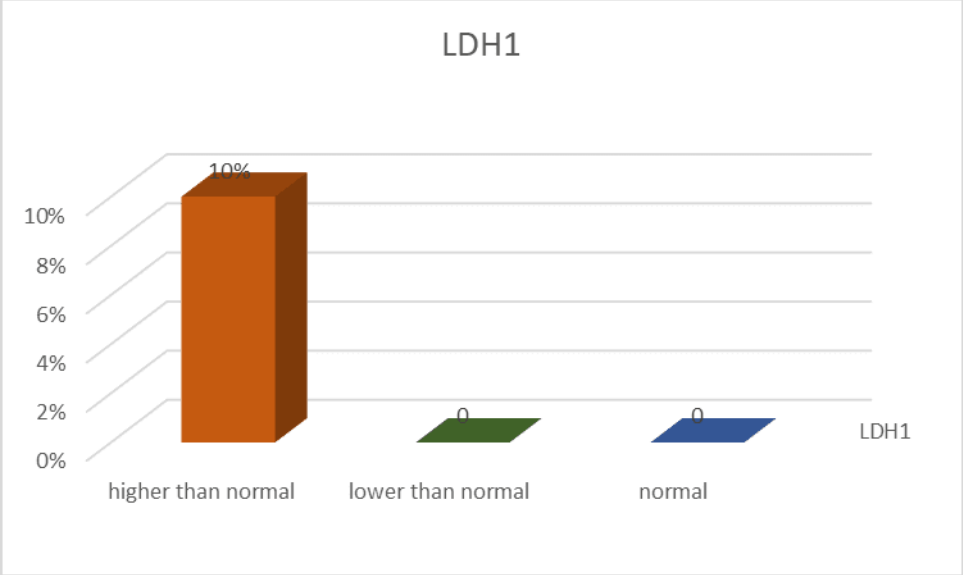

Figure 4f: LDH1 levels

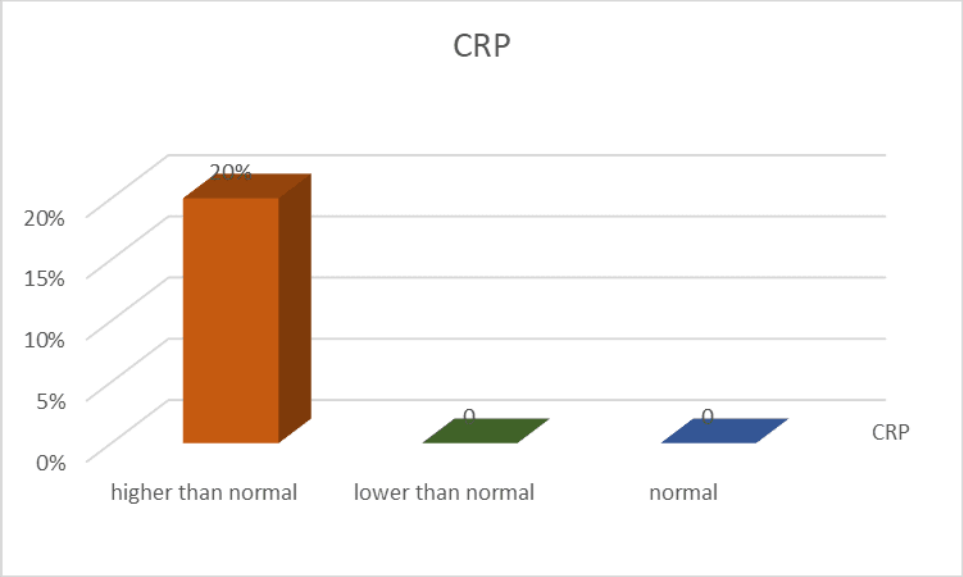

Figure 4g: C-reactive proteins (CRP) levels

Moreover, we have also analyzed the prescription pattern writing of clinicians, which are shown in below mentioned tables (Table 5a to 5c). Prescriptions from the record files revealed that 8% of the prescriptions had non-proprietary i.e., generic names on it. Majority of the prescriptions had brand names i.e., proprietary drug names [Table 5a/Figure 5].

Table 5a: Pattern of prescriptions writing in geriatric patients

Proprietary and non- proprietary drugs in prescription writing	Number of patients (n=50)	Percentage (%)
Generic name	4	8%
Brand name	46	92%

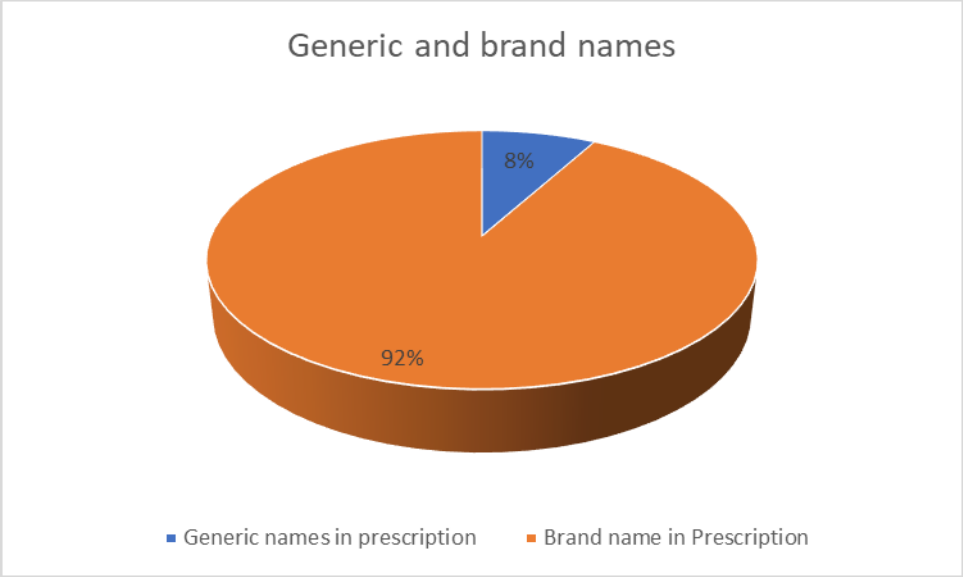

Figure 5a: Pattern of prescription writing

Table 5b: Pattern of prescription writing – Genderwise distribution

Gender wise proprietary and non proprietary drugs in prescription writing	Males (n=26)	Percentage males (%)	Females (n=24)	Percentage Females (%)
Generic names in Prescription	1	3.84%	3	12.50%
Brand name in Prescription	25	96.15%	21	87.50%

Table 5c: Pattern of prescription writing among geriatric age groups

Geriatric distribution of proprietary and non proprietary drugs in prescriptions	Age 65-69 years (n=25)	Percentage 65-69 yrs (%)	Age 70-74 years (n=11)	Percentage 70-74yrs (%)	Age 75-79 years (n=10)	Percentage 75-79yrs (%)	Age 80-84 years (n=4)	Percentage 80-84 yrs (%)
Generic names in Prescription	2	8%	1	9.09%	1	10%	0	0
Brand name in Prescription	23	92%	10	90.90%	9	90%	4	100%

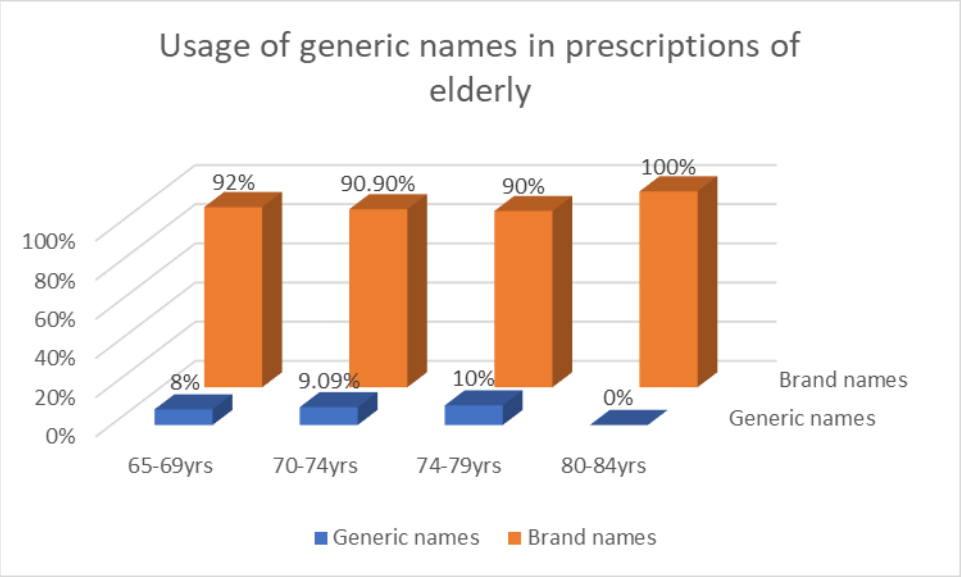

Figure 5b: Pattern of prescription writing among geriatric age groups

We also studied the pharmacokinetics, such as route of administration [Table 6a to 6c]. It was observed that the main route of administration amongst overall drugs prescribed were oral route, followed by both oral and parenteral, followed by parenteral only route.

Table 6a: NSAIDs and other Drugs administered through various routes

Various routes of drug administration in elderly	Number of patients (n=50)	Percentage (%)
Route of administration ORAL	32	64%
Route of administration PARENTERAL	3	6%
Route of administration both oral and parenteral	15	30%

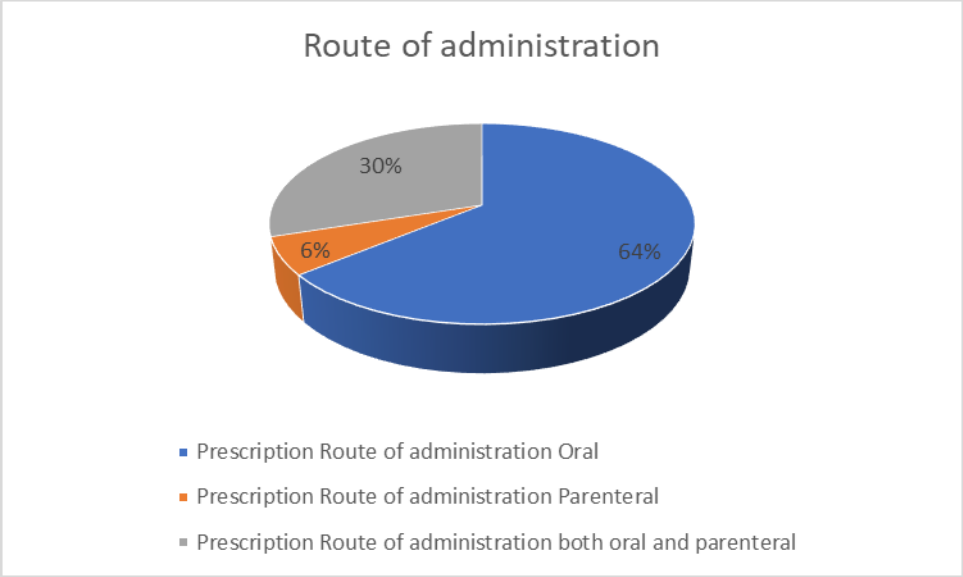

Figure 6a: NSAIDs and other Drugs administered through various routes

Table 6b: Gender wise Routes of Administration

Routes of drug Administration	Males (n=26)	Percentage males (%)	Females (n=24)	Percentage Females (%)
Oral	18	69.23%	14	58.33
Parenteral	0	0	3	12.50%
Both oral and parenteral	8	30.76%	7	29.16%

Table 6c: Age group wise distribution of routes of administration

Routes of drug administration	Age 65-69 years (n=25)	Percentage 65-69 yrs (%)	Age 70-74 years (n=11)	Percentage 70-74yrs (%)	Age 75-79 years (n=10)	Percentage 75-79yrs (%)	Age 80-84 years (n=4)	Percentage 80-84 yrs (%)
Oral	17	68%	8	72.72%	4	40%	3	75%
Parenteral	0	0	1	9.09%	2	20%	0	0
Both oral and parenteral	8	32%	2	18.18%	4	40%	1	25%

DISCUSSION & CONCLUSION

Our present retrospective study was carried out in a rural tertiary care teaching hospital located in Piparia village of Gujarat. Out of total 50 patient case files filled from the record section of Dhiraj hospital, we studied the majority of prescriptions of patients admitted in orthopedic and medicine wards. In this study with aim to find out the usage of NSAIDs, the most significant outcome was, Aspirin, paracetamol, diclofenac and combination of paracetamol + diclofenac was found to be the main NSAIDs drugs prescribed to the geriatric patients in medicine and orthopedic wards. The tendency of using proprietary names was reported to be significantly higher than that of non-proprietary names. The fixed dose combinations in the prescriptions overall are found to be 34%. Among all the prescriptions with fixed dose combinations, 94.11% were with polypharmacy, 5.88% were without polypharmacy. This reflects those prescriptions with polypharmacy have more fixed dose combinations. Moreover, among elderly groups, highest prescribed fixed dose combinations were found in age groups 80-84 years. While 10% adverse drug events were found in the study population of 50 elderly cases, all of them were found in prescriptions with polypharmacy, i.e., 11.62% of polypharmacy cases had adverse drug events while none were found in those without polypharmacy. In prescriptions, generic names were prescribed in 8% while brand names were prescribed in 92% of prescriptions. Nearly 64% had oral route, 6% parenteral and 30% both oral and parenteral routes of administration in prescriptions. Adverse drug events of gastric reflux and acidity is found in 10% of cases.

Although number of days of stay in hospital and comorbidities were also found more in polypharmacy, it remains unclear if the prescribing of polypharmacy among such comorbid and chronically ill patients could be claimed to be unnecessary or necessary. More such studies focusing on the rationality of polypharmacy among such groups is required to develop an in-depth knowledge regarding this aspect. Hence it can be concluded that the usage of NSAIDs aspirin, acetaminophen and diclofenac are frequent among the elderly patients in medicine and orthopedics departments. Thus, only judicious concurrent use of multiple drugs should be promoted keeping mind the health, financial and comorbidity related factors in elderly.

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