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STUDY ON DRUG EVALUATION AND UTILIZATION OF NON STEROIDAL ANTI INFLAMMATORY DRUGS: PROSPECTIVE OBSERVATIONAL

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ABSTRACT
Non-Steroidal Anti-Inflammatory Drugs are the class of drugs that provide analgesic, antipyretic(fever reducing) and in higher doses anti-inflammatory effects. The term "Nonsteroidal" distinguishes these drugs from steroids, which among broad range of other effects have a similar Eicosanoids depressing anti-inflammatory effect. As analgesics, Nonsteroidal anti-inflammatory drugs are unusual in that they non-narcotic. Nonsteroidal anti-inflammatory drugs the most highly prescribed drugs in the world, and also prevalently used in the age group of (0-10) years patients. The Paracetamol and Diclofenac were most frequently prescribed for the management of Pyrexia, Pain, Inflammation and Traumatic injury. Their Analgesic, Anti-inflammatory and Antipyretic actions may be beneficial, they are associated with severe side effects including gastrointestinal injury and peptic ulceration. The monotherapy with single Nonsteroidal anti-inflammatory drug were preferred mode of therapy via parenteral and oral routes. Nonsteroidal anti-inflammatory drugs were mostly co-prescribed with proton pump inhibitors. Use of Nonsteroidal anti-inflammatory drugs are more than Cox-2 inhibitors. Ketorolac was the most frequently used drug 29.3% in general hospitals and Diclofenac used at the rate 50% in specialized hospitals. The purpose of Drug Utilization and Evaluation is to ensure that drugs are used appropriately, safely and effectively to improve patient health status. This project also provides the information on different preventive measures prescribed to minimize such adverse effects and analyses the new suggested strategies for development of Novel drugs to maintain the Anti-inflammatory functions of Nonsteroidal anti-inflammatory drugs along with effective gastrointestinal protection.

KEYWORDS: Analgesic, Anti-inflammatory, Nonsteroidal anti-inflammatory drugs, GI damage.

INTRODUCTION
Drug Use Evaluation (DUE) is defined as an authorized, structured, ongoing review of practitioner prescribing, pharmacist dispensing, and patient use of medications. The World Health Organization (WHO) in 1997 defined drug utilization as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.

DUE is an ongoing, systematic process designed to maintain the appropriate and effective use of drugs. It involves a comprehensive review of patient's prescription and medication data before, during, and after dispensing in order to assure appropriate therapeutic decision making and positive patient outcomes. Pharmacists participating in DUE programs can directly improve the quality of care for patients, individually and as populations, by preventing the use of unnecessary or inappropriate drug therapy and by preventing adverse drug reactions.

The purpose of a DUE is to ensure that drugs are used appropriately, safely, and effectively to improve patient health status. In addition, continual improvement in the appropriate and effective use of drugs has the potential to lower the overall cost of care.

DUE allows the pharmacist to document and substantiate the benefit of pharmacy intervention in improving therapeutic and economic outcomes. Drug use is a complex process. In any country a large number of socio-cultural factors contribute to the ways drugs are used. In India, these include national drug policy, illiteracy, poverty, use of multiple health care systems, drug advertising and promotion, sale of prescription

drugs without prescription, competition in the medical and pharmaceutical market place and limited availability of independent, unbiased drug information. The complexity of drug use means that optimal benefits of drug therapy in patient care may not be achieved because of underuse, overuse or misuse of drugs. Inappropriate drug use may also lead to increased cost of medical care, antimicrobial resistance, adverse effects and patient mortality. Hence in recent years studies on drug utilization have become a potential tool to be used in the evaluation of health system.

Acute increases in antibiotic resistance may be due to antibiotic selection pressures, over-crowding and other environmental changes, all of which are present in our setting. The most resistant organisms are found in units where patients are immune- compromised, are subject to invasive procedures or remain for long periods institutions elsewhere in the world have enhanced patient care through therapeutic optimization of the use of antimicrobial agents through the use of antibiotic restriction policies implemented widely throughout the hospital. Appropriate use of antibiotics is central to limiting the development and the spread of resistant bacteria in hospitals and communities.

Thus DUE plays a key role in helping the healthcare system to understand, interpret and improve the prescribing, administration and use of medications. The principal aim of DU research is to facilitate rational use of drugs, which implies the prescription of a well documented drug in an optimal dose on the right indication, with correct information and at an affordable price. It also provides insight into the efficacy of drug use i.e. whether a certain drug therapy provides value for money. DU research can thus help to set priorities for the rational allocation of health care budgets.

NSAIDs

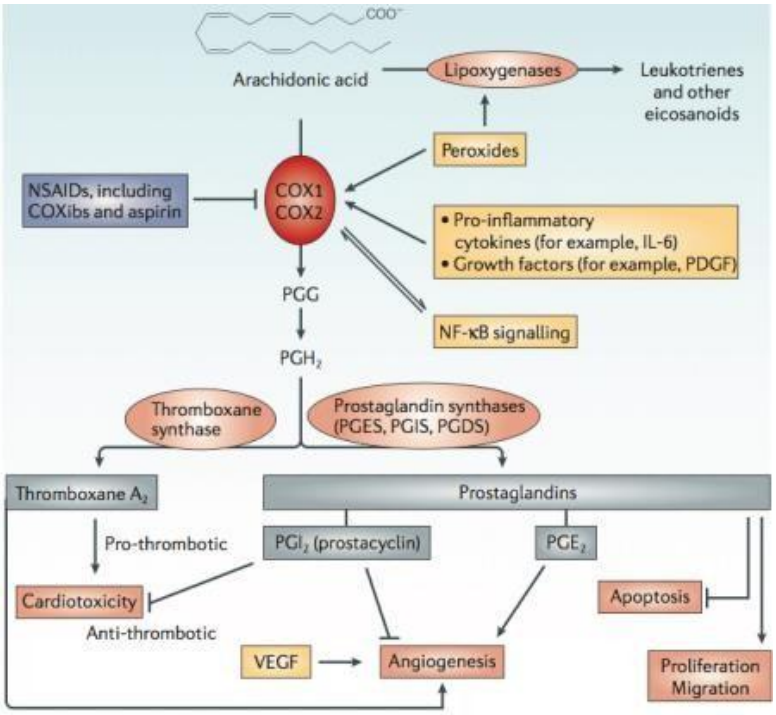
Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of drugs that provide analgesic & antipyretic effects, & in higher doses, anti-inflammatory effects.

Classification

A. Non-selective COX Inhibitors:
1. Salicylic acid derivatives: Aspirin
2. Para-aminophenol derivatives: Paracetamol
3. Propionic acid derivatives: Ibuprofen, Naproxen, Ketoprofen & Flurbiprofen.
4. Fenamate: Mefenamic acid
5. Enolic acid derivatives: Piroxicam & Tenoxicam.
6. Acetic acid derivatives: Ketorolac, Indomethacin & Nabumetone.
7. Pyrazolone derivatives: Phenylbutazone & Oxyphenbutazone.

B. Preferential COX-2 inhibitors:
- Nimesulide, Diclofenac, Aceclofenac, Meloxicam, Lornoxicam & Etodolac.

C. Selective COX-2 inhibitors:
- Celecoxib, Etoricoxib & Parecoxib.



Mechanism Of Action Of NSAIDS

Common side effects with NSAIDs are Indigestion, stomach ulcer, Anemia, Gastrointestinal perforation.

RESULTS

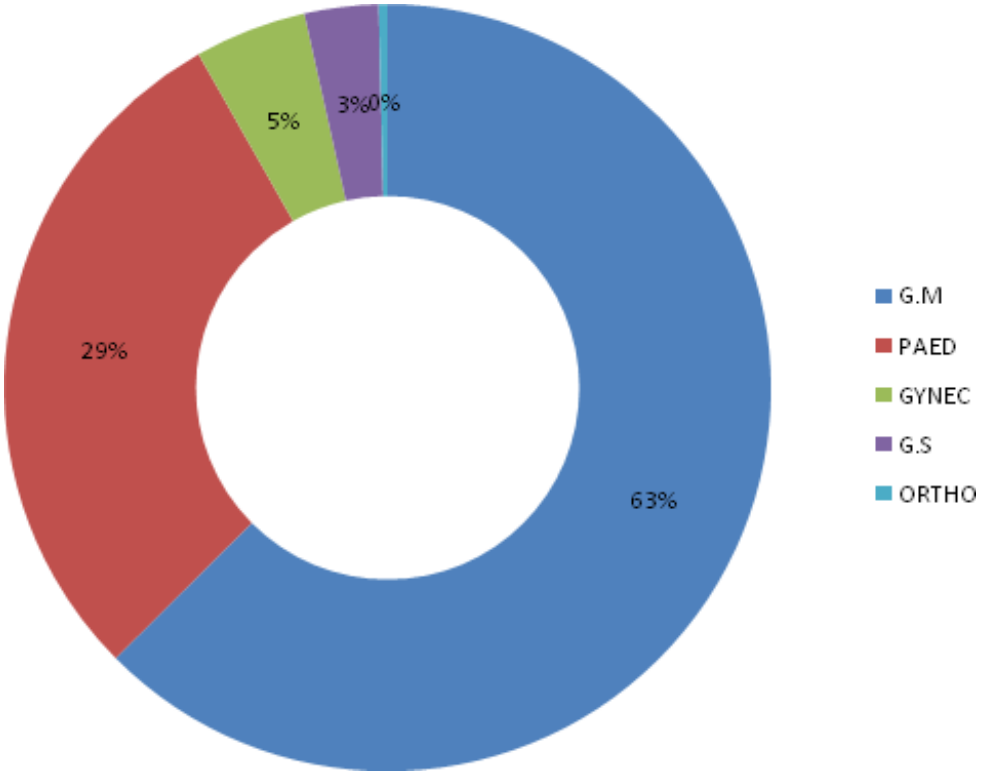
The clinical study was carried out with 300 patients who were prescribed with NSAIDs in the department of General medicine, Pediatrics, Gynecology,

Orthopedicsand Surgery.

WARD WISE DISTRIBUTION

Out of 300 patients, 57% were admitted in General Medicine, 31% in Pediatric, 25% in Gynecology, 10% in surgery & 0.4% in orthopedic.

WARD	NO OF PATIENTS	PERCENTAGE (%)
General Medicine	181	60.33
Pediatric	93	31
Gynecology	15	5
General surgery	10	3.3
Orthopedic	1	0.4

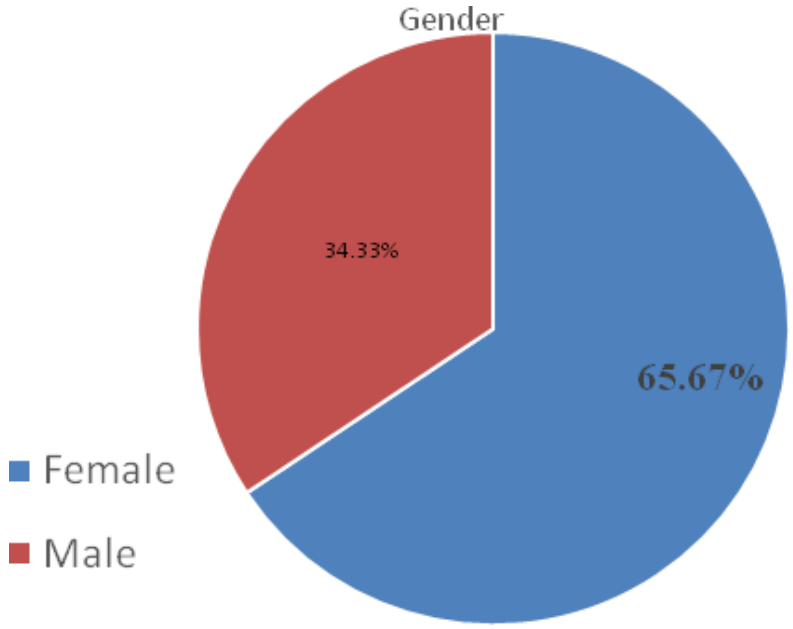


Ward Wise Distribution in Study Population

GENDER DISTRIBUTION

In the study population of 300 patients, 197 were Female patients and 103Male patients. It indicates Female patients were found to be more (65.67%).

GENDER	NO.OF PATIENTS	PERCENTAGE (%)
Female	197	65.67
Male	103	34.33

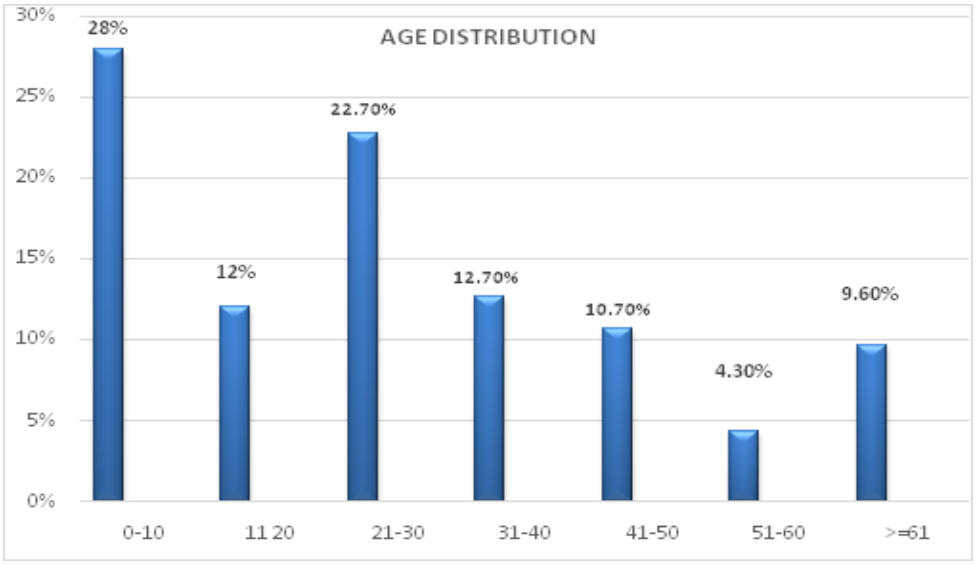


Gender distribution of Study population

AGE DISTRIBUTION

Out of 300 patients, 84(28%) were between 0-10years were more whereas thepatients belonging to age group of 51-60(13%) years were less.

AGE GROUP(YRS)	NO.OF PATIENTS	PERCENTAGE (%)
0-10	84	28
11-20	36	12
21-30	68	22.7
31-40	38	12.7
41-50	32	10.7
51-60	13	4.3
=61	29	9.6

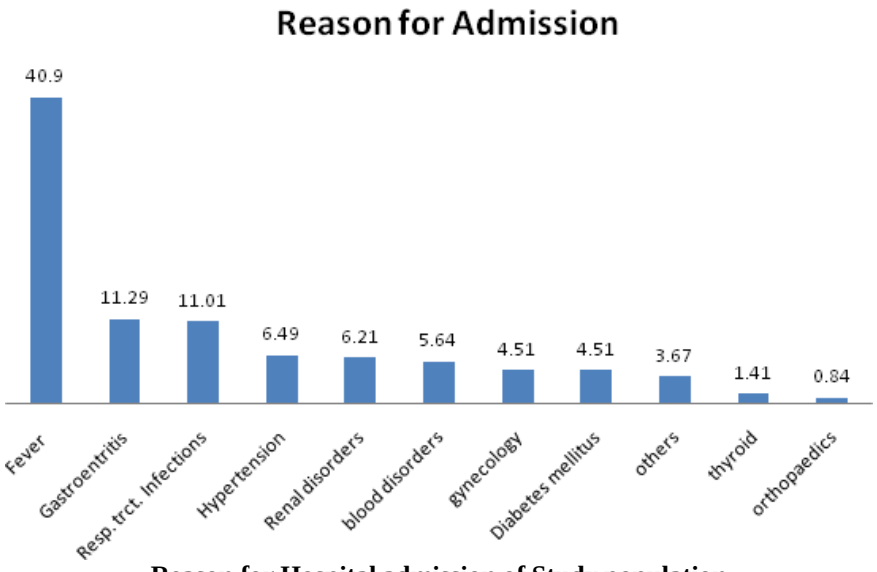


Age Distribution of Study population

REASON FOR ADMISSION

In our study, we could observe fever (40.9%), epilepsy (3.38), respiratory tract infection (11.01%), renal disorders (6.21%), blood disorders (5.64%), gynecology (4.51%), thyroid (1.41%), hypertension (6.49%), diabetes mellitus (4.51%), orthopedics (0.84%), gastro enteritis (11.29), others (3.67%).

REASON FOR ADMISSION	NO.OF.PATIENTS	PERCENTAGE (%)
Fever	145	40.9
Gastro entritis	40	11.29
Respiratory tract infection	39	11.01
Hypertention	23	6.49
Renal disorders	22	6.21
Blood disorders	20	5.64
gynecology	16	4.51
Diabetes mellitus	16	4.51
Others	13	3.67
Thyroid disorders	5	1.41
orthopaedics	3	0.84

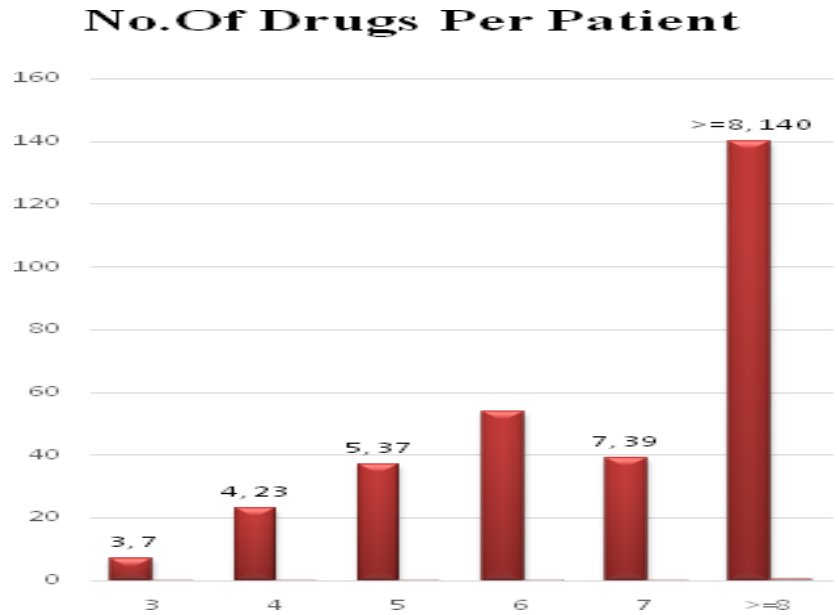


Reason for Hospital admission of Study population

NUMBER OF DRUGS PER PATIENT

Out of 300 patients, ≥ 8 drugs were prescribed for 46.7%, 5 drugs for 12.3% whereas 3(2.3%) drugs were prescribed less.

NO. OF DRUGS PER PATIENT	NO. OF PATIENTS	PERCENTAGE (%)
3	7	2.3
4	23	7.7
5	37	12.3
6	54	18
7	39	13
=8-19	140	46.7

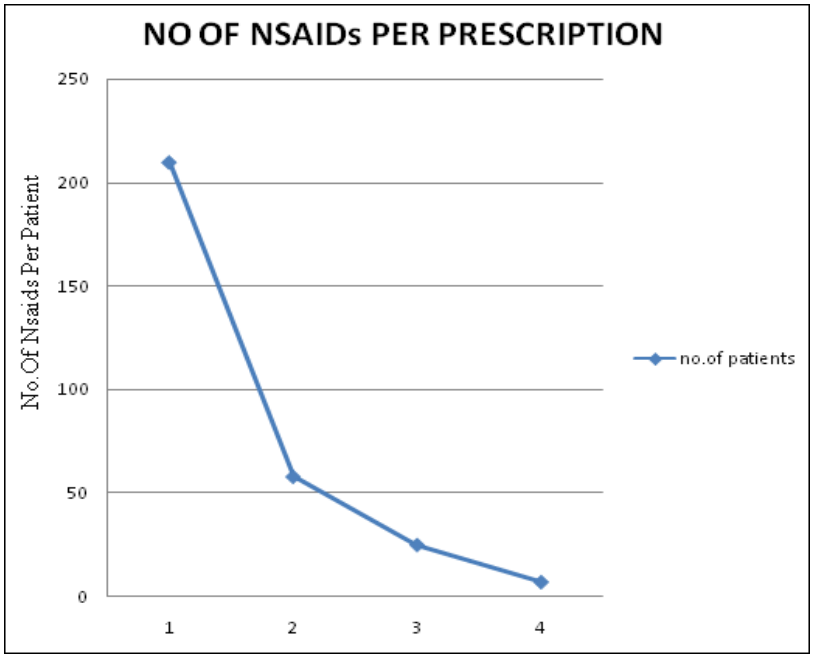


No. of Drugs Per Patient in the Study Population

No. OF NSAID's PER PATIENT

In our study, 70% patients were prescribed with a single NSAID and 2.4% with 4NSAIDs.

NO. OF NSAIDs	NO OF PATIENTS	PERCENTAGE (%)
1	210	70
2	58	19.3
3	25	8.3
4	7	2.4

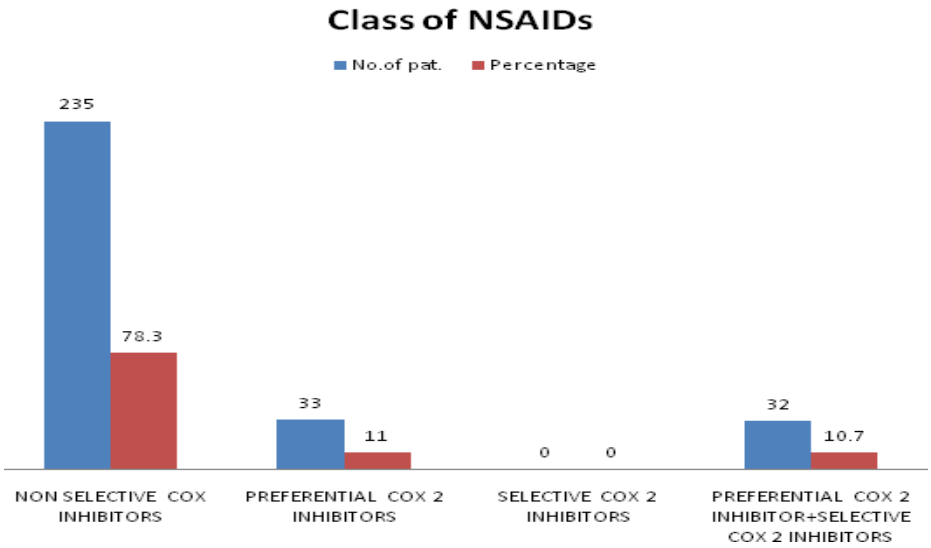


No. of NSAIDs Per Prescription in the study population

CLASS OF NSAIDs PRESCRIBED TO STUDY POPULATION

In our study, Preferential Cox 2 inhibitors were prescribed for 11%, Non-Selective Cox inhibitors for 78.3% & combination of both were 10.7%.

NSAIDs CLASS	NO OF PATIENTS	PERCENTAGE (%)
Non Selective Cox Inhibitors	235	78.3
Preferential Cox 2 Inhibitors	33	11
Selective Cox 2 inhibitors	0	0
Preferential Cox 2 + Non Selective Cox Inhibitors	32	10.7

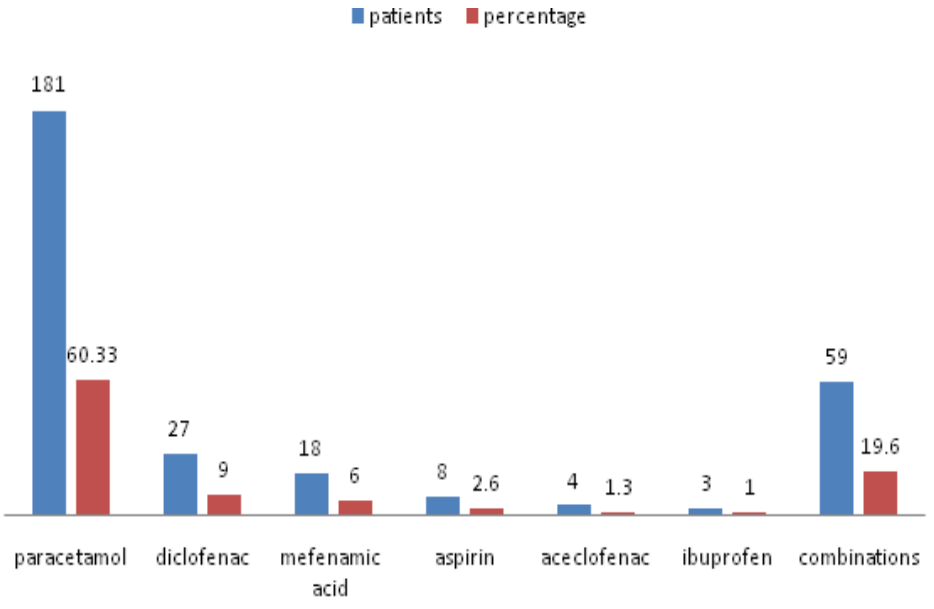


Class of NSAIDs Prescribed in the Study population

DISTRIBUTION OF PRESCRIBED NSAIDs IN STUDY POPULATION

In our study, the most commonly prescribed NSAID was paracetamol for 60.33%, followed by diclofenac for 9% patients Although some patients were prescribed with combinations as follows.

NSAIDs	NO. OF PATIENTS	PERCENTAGE (%)
Paracetamol	181	60.33
Diclofenac	27	9
Mefenamic acid	18	6
Aspirin	8	2.6
Aceclofenac	4	1.3
Ibuprofen	3	1
Combinations	59	19.6



Distribution of Prescribed NSAIDs in study population

Combinations of NSAIDs

Out of 300 patients, 59 patients were prescribed with combinations of various NSAIDs such as diclofenac, paracetamol, ibuprofen, mefenamic acid, aceclofenac, aspirin, dicyclomine, ketorolac and piroxicam.

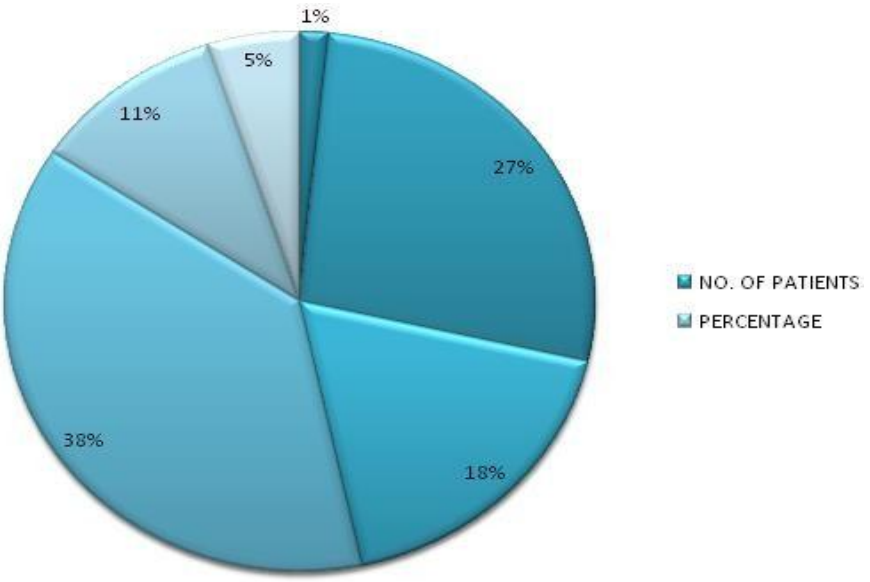
Combination of NSAIDs	No. of patients	Percentage(%)
Diclofenac + Paracetamol	12	4
Ibuprofen+paracetamol	8	2.6
Paracetamol+mefenamic acid	8	2.6
Aceclofenac + Paracetamol	6	2
Pcm+diclofenac+ibuprofen	5	1.6
Paracetamol+aspirin	4	1.33
Paracetamol+dicyclomine	3	1
Diclofenac+ketorolac	3	1
Paracetamol+piroxicam	1	0.3
Aspirin+diclofenac	1	0.3
Aceclofenac+diclofenac	1	0.3
Aceclofenac+pcm+mefenamicacid	1	0.3
Pcm+mefenamic acid+diclofenac	1	0.3
Pcm+diclo+aceclofenac	1	0.3
Pcm+ibuprofen+mefenamic acid	1	0.3
Pcm+mefenamic acid+aspirin	1	0.3
Pcm+aspirin+aceclofenac	1	0.3
Mefenamic acid+ketorolac+diclofenac	1	0.3

Distribution of Prescribed Combinations of NSAIDs in study population

DURATION OF NSAIDs USE

Out of 300 patients, the duration of use of NSAIDs for 1 day (1.6%), 3 days (27%), 4 days (18%), 5 days (37.7%), 6 days (10.7%) and 5% patients for ≥7 days were observed.

DURATION OF USE OF NSAIDS	NO.OF PATIENTS	PERCENTAGE (%)
1 day	5	1.6
3 days	81	27
4 days	54	18
5 days	113	37.7
6 days	32	10.7
=7 days	15	5

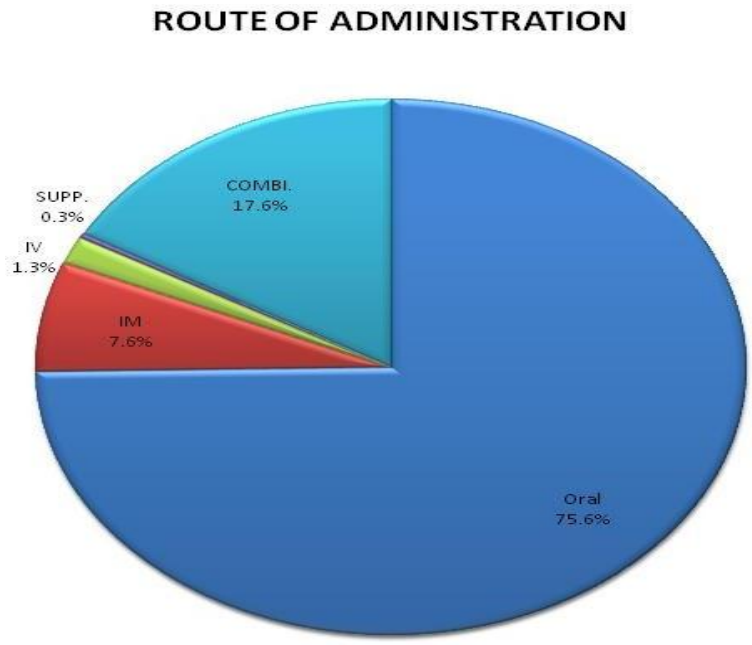


Duration of NSAIDs use in Study population

ROUTE OF ADMINISTRATION

Out of 300 patients 224 patients (74.6%) with ORAL, 20 patients (6.6%) with IM 5 patients(1.66%) with IV, 1 patient (0.3%) with SUPPOSITORY, 50 patients (16.66%) were prescribed with COMBINATIONS of route of administration.

ROUTE OF ADMINISTRATION	NO OF PATIENTS	PERCENTAGE (%)
ORAL	224	74.6
IM	20	6.6
IV	5	1.66
SUPPOSITORY	1	0.3
COMBINATIONS	50	16.66



Route of Administration given in the Study population

COMBINATIONS OF ROUTE OF ADMINISTRATIONS OF NSAIDs

ROUTE OF ADMINISTRATION	NO.OF PATIENTS	PERCENTAGE(%)
IV+ORAL	15	5
IM+ORAL	20	6.6
ORAL+IM+IV	4	1.3
IM+IV	3	1
ORAL+SUPPOSITORY	3	1
IV+SUPPOSITORY	3	1
ORAL+TOPICAL	1	0.3
SUPPOSITORY+IV+ORAL	1	0.3

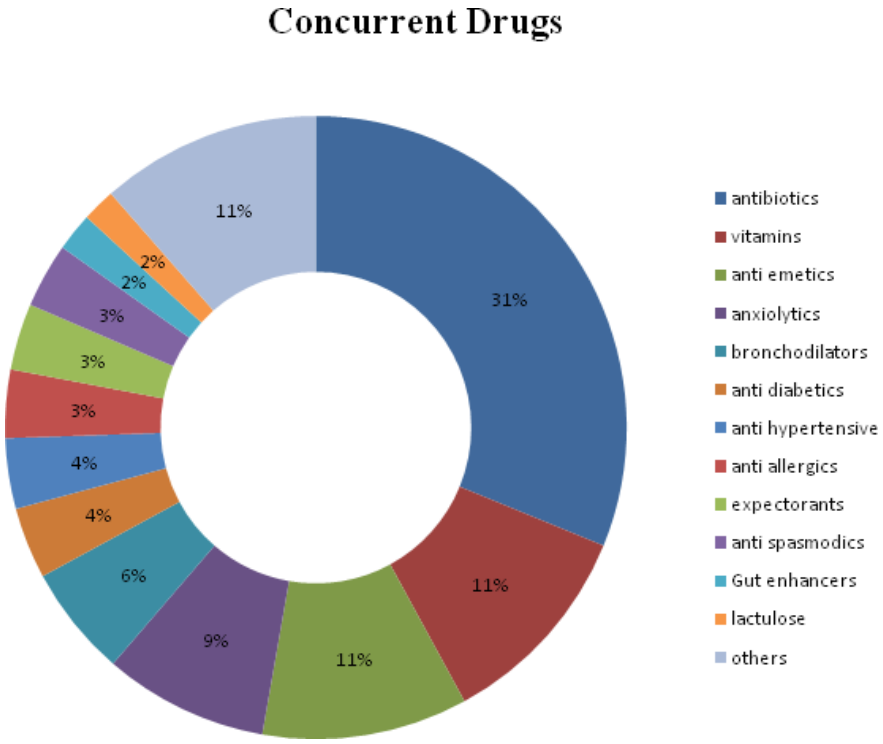
Combinations Of Route Of Administration Given In The Study population

CONCURRENT DRUGS PRESCRIBED

Major prescriptions of NSAIDs were antibiotics (33.76%) followed by vitamins (11.78%). Other contents of prescription were bronchodilators, antiemetics, antihypertensives, antidiabetics, corticosteroids, anxiolytics and others.

	PRESCRIBED	PATIENTS	
1.	Antibiotics	361	33.76
2	Vitamins	126	11.78
3	Anti emetics	124	11.59
4	Anxiolytics	99	9.26
5	Bronchodilators	67	6.26
6	Antidiabetics	43	4.02
7	Antihypertensives	42	3.92
8.	Anti allergics	41	3.83
9	Expectorants	40	3.74
10.	Anti spasmodics	39	3.64
11.	Gut enhancers (lactobacillus)	23	2.15
12.	Lactulose	20	1.87

	OTHERS		
13	Calcium	7	0.65
14	Corticosteroids	7	0.65
15	Drugs related to cardiology	6	0.56
16	Drugs related to thyroid disorders	6	0.56
17	Hepato protectives	5	0.46
18	Amino acids	4	0.37
19	Coagulants	3	0.28
20	Hormones	2	0.18
21	Hypolipidaemics	2	0.18
22	Anti vertigo drugs	2	0.18

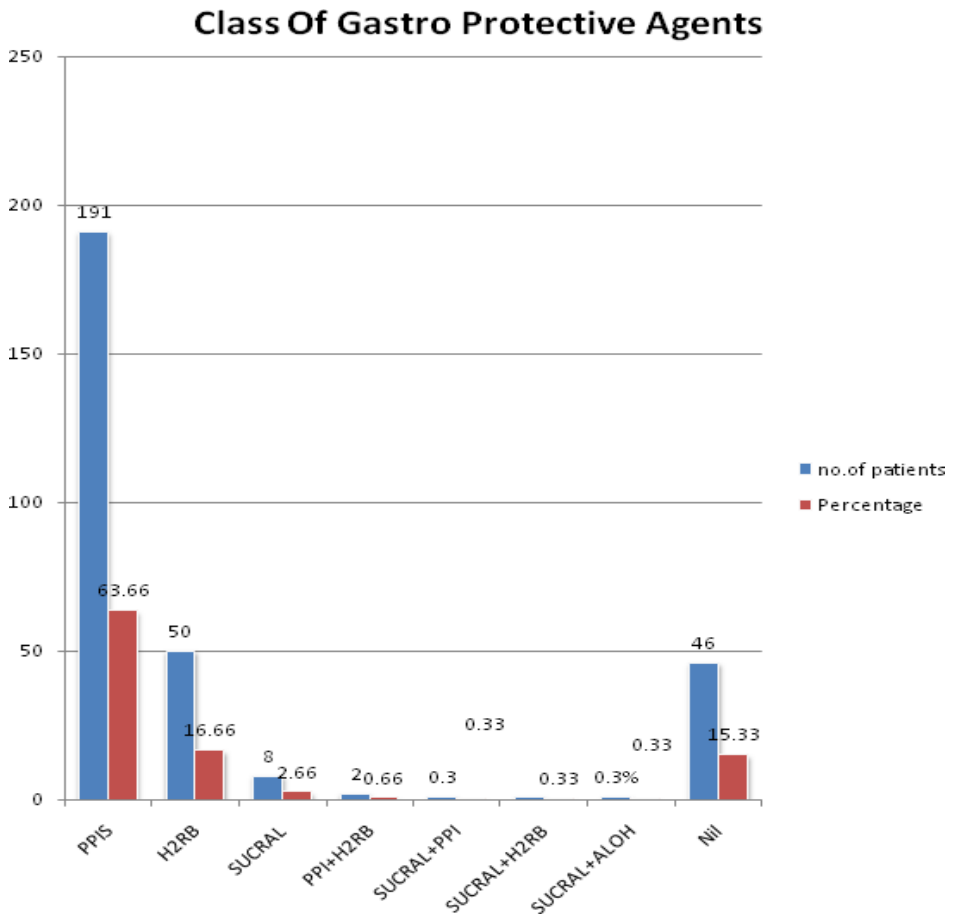


Concurrent drugs prescribed in Study population

CLASS OF GASTROPROTECTIVE AGENTS

Among 300 patients, 254 patients were prescribed with gastro protective agents where as 46 patients were not prescribed with gastroprotectives, out of 254 patients, 63.66% of patients were prescribed with proton pump inhibitors, 16.66% of patients with H2 receptor antagonist, 2.66% of patients with sucralfate, 0.66% of patients with ranitidine + pantoprazole, 0.3% of patients with sucralfate + pantoprazole, 0.3% of patients with sucralfate + ranitidine and, 0.3% of patients with sucralfate + aluminium hydroxide.

S.NO.	CLASS	NO. OF PATIENTS	PERCENTAGE (%)
1.	Proton pump inhibitors	191	63.66
2.	H 2 receptor antagonist	50	16.66
3.	Sucralfate	8	2.66
4.	Ranitidine+pantoprazole	2	0.66
5.	Sucralfate+PPIS	1	0.33
6.	Sucralfate + h2 recep blockers	1	0.33
7.	Sucralfate + aluminium hydroxide	1	0.33
8.	Nil	46	15.33



Class of Gastroprotective agents prescribed in study population

DRUG INTERACTIONS

In our study a few major and moderate drug interactions were observed.

S.NO.	INTERACTING DRUGS	SEVERITY	CLINICAL EFFECT	CLINICAL MANAGEMENT
1	KETOROLAC & DICLOFENAC	MAJOR	Black or bloody stools , coughing with stools & shallow breathing	Concurrent use of ketorolac with other NSAIDs is considered contraindicated.
2	AMIKACIN & DICLOFENAC	MODERATE	Diclofenac increases the side effects of amikacin	Discontinue diclofenac
3	DICLOFENAC & CIPROFLOXACIN /OFLOXACIN	MODERATE	Diclofenac increases the risk of seizures with high dose of ciprofloxacin	Blood glucose levels should be monitored
4	DICLOFENAC & TELMISARTAN	MODERATE	Lowers blood pressure and impairs kidney function	Monitor the blood pressure and increase the dose of Atenlol
5	ASPIRIN & TELMISARTAN	MODERATE	Lowering the blood pressure (deteriorates renal function)	Replacement of the antibiotic if possible.
6	MEFENAMIC ACID & GLIPIZIDE	MODERATE	Increase the effect of glipizide(risk of hypoglycemia)	
7	MEFENAMIC ACID & ATENOLOL	MODERATE	Decrease in the effect of Atenolol pharmacodynamically	
8	MEFENAMIC & CIPROFLOXACIN	MODERATE	Increase the effect of Ciprofloxacin	

Drug Interactions noted in the Study population

DISCUSSION

A prospective observational study, "A study on drug evaluation and utilization of non steroidal anti inflammatory drugs**"** was conducted in 300 bedded tertiary care teaching hospital including the inpatients from orthopedic, surgery, general medicine, pediatric and gyneacology departments over a period of six months. The data was collected from 300 in-patients using specially designed data collection form.

Like most of studies have shown that more female patients use NSAIDs than male, our present study also showed that more females (197) are using NSAIDs than males (103) out of 300 patients.

In this study, majority of patients using NSAIDs were between the ranges of 0-10yrs (84 patients), 21-30yrs (68 patients) and 31-40yrs (38patients). It shows that NSAIDs areused mainly in age group of 0-10 years. Out of 300 patients, majority were from general medicine (66.3%), paediatrics(31%), gynaecology (5%) and surgery department (3.3%). However only 1 patient was from orthopedic department. **Pyrexia** was the major clinical complaint of the patients (40.9n%) besides gastroenteritis (11.29%) respiratory tract infections (11.01%).

Out of 300 patients, 153 patients were prescribed with ≥ 7drugs followed by 78 patients with 4 drugs and 77 patients with 5 drugs per prescription. However, most of the patients were prescribed with single NSAIDs as monotherapy, although some patients were prescribed with combinations of NSAIDs such as Ibuprofen+paracetamol, Paracetamol+mefenamic acid, Aceclofenac + Paracetamol, Pcm+diclofenac+ibuprofen, Paracetamol+aspirin, Paracetamol+dicyclomine.

It is observed from the study that, most of the patients (78.3%) were prescribed with non selective COX inhibitors and few patients (11.0%) were prescribed with preferential COX2 inhibitors and remaining were prescribed with combination of Non Selective Cox Inhibitors And Preferential Cox 2 Inhibitors. However the selective COX 2 inhibitors were not prescribed. Although traditional NSAIDs including preferential COX 2 inhibitors and non selective COX inhibitors are associated with high rate of GI complications, but possess low risk of cardiovascular complications than that of selective COX 2 inhibitors. Moreover several studies have revealed that coxibs use has been restricted to avoid the risk of heart attack and stroke. Besides the cost of coxibs is also higher than traditional NSAIDs. Hence the non-prescription of selective COX 2 inhibitors observed from the study is rational.

It is observed from the study that, Paracetamol (60.33%) and Diclofenac (9%) were mostly prescribed and least prescribed NSAIDs were Aceclofenac and Ibuprofen.

In our study, most of the NSAIDs were prescribed via oral route (74.6%), parentral route (8.2%) and combinations of route of administrations (16.6%). However the suppository NSAIDs (0.3%) and topical + suppository NSAIDs (0.3%) were least prescribed. Topical route causes a high local concentration in cutaneous and subcutaneous area of the body with low systemic delivery, thereby significantly improving therapeutic efficacy and minimizing systemic side effects.

To manage NSAIDs associated GI adverse effects, a PPI, H2 antagonist or local acting antacids must be co-prescribed with NSAIDs. In the present study more than 80% of patients were co-prescribed with gastroprotective agents along with NSAIDs, out of which 63.66% were prescribed with proton pump inhibitors and 16.66% with H2 receptor antagonist and 2.66% of patients were prescribed with sucralfate. The other concurrently prescribed drugs include antibiotics (33.7%) and multivitamins (11.7%), anti emetics (11.5%) anxiolytics (9.2%), and rest includes cariotonis, aminoacids, anti hypertensives etc.

In the study major drug interactions were found between NSAIDs such as ketorolac & diclofenac, moderate drug interactions were between NSAIDs & Antibiotics. No Adverse drug reactions were reported during the study.

CONCLUSION

In present study NSAIDs were more prevalently used in age group 0-10 years and mostly prescribed in female patients. Paracetamol and diclofenac were most frequently prescribed for the management of pain, inflammation and pyrexia. NSAIDs were mostly co prescribed with PPIs. The monotherapy with single NSAID was preferred mode of therapy via parenteral and oral therapy.

NSAIDs are vital for clinical management of wide range of pain and inflammatory conditions, but it is mostly accompanied by gastrointestinal complications. In the present study, the gastro protective agents were widely prescribed for prevention and healing of NSAIDs associated ulcers or other GI complications.

In the present study, the prescription of NSAIDs is found to be rational. However to ensure safe, effective and well balanced therapeutic management of this NSAIDs, both patients and prescribers should be more aware of the appropriate dose, dosage regimen and overall indications.

Drugs can be useful tools in the prevention and management of symptoms and disease, but if not used properly, they may be harmful and cause new symptoms or produce suboptimal effects. The drug utilization problems are common and have significant clinical and economic complications. Hence the support and involvement of pharmacist along with medical staff is essential for rational drug utilization.

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