

**PRESCRIPTION PATTERN ANALYSIS OF NSAIDS AND
MULTIVITAMINS AMONG THE SPECIALIST DOCTORS OF
DIFFERENT AREAS IN BANGLADESH**

Submitted by

Md. Monowar zahid

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In partial fulfillment of the requirements for the award of the degree

Bachelor of Pharmacy

Under The Guidance of

Mohammed Faisal Bin Karim

Senior Lecturer, Department of Pharmacy

East West University

DECLARATION BY THE RESEARCH CANDIDATE

I, Md. Monowar Zahid, here by declare that the dissertation entitle Prescription Pattern Analysis of NSAIDs and Multivitamins in Different Area of Bangladesh "" submitted by me to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the award of the degree of Bachelor of Pharmacy (Honors) is a record of original research work carried out by me during 2015-2016 (July —April) under the supervision and guidance of Mohammed Faisal Bin Karim Senior Lecturer Dept. of Pharmacy, East West University.

Signature of the candidate

Md. Monowar Zahid

2012-3-70-036

CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation " Prescription Pattern Analysis of NSAIDs and Multivitamins in Different Area of Bangladesh" submitted to the department of pharmacy, East West University was carried out by Md. Monowar Zahid (ID: 2012-3-70-036) in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy.

Supervisor

Mohammed Faisal Bin Karim

Senior Lecturer

Department Of Pharmacy

East West University

Aftabnagar, Dhaka, Bangladesh

ENDORSEMENT BY HEAD OF THE DEPARTMENT

This is to certify that the subject " Prescription Pattern Analysis of NSAIDs and Multivitamins in Different Area of Bangladesh" submitted to the Department of Pharmacy, East West University in partial fulfillment of the requirements of the degree of Bachelor of Pharmacy was carried out by Md. Monowar Zahid (ID: 2012-3-70-036) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all the sources of information is duly acknowledged.

Dr. Shamshun Nahar Khan

Chairperson

Department of Pharmacy

East West University

Aftabnagar, Dhaka, Bangladesh

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DEDICATION

This Research Paper is Dedicated To

My Beloved parents

ABSTRACT

Irrational drug use and inappropriate prescription of drugs are major problems in developing countries, and so drug use patterns need to be evaluated. The objective of the study was to investigate the prescribing patterns of NSAIDs and multivitamins in the Out-patient hospital and Pharmacy Department of different area of Bangladesh. Prescriptions were obtained from patients visiting private and public hospitals in different areas of Dhaka and outside of Dhaka like khulna, Barisal,shylet,Chittagong and others. . Here the evaluation of prescription was based on the % of NSAID drugs prescribed,% of EDL drugs prescribed among NSAID,% ,% of different NSAID generic prescribed, % of different companies NSAID drug prescribed. The Total number of prescription was 1600,. The extent of prescribing drugs by generic name was almost zero, and the percentage of prescription of essential drugs was 54.98%. NSAIDs were prescribed in 33.8% of the prescriptions, with aspirin , paracetamol and diclofenac being the most frequently prescribed NSAIDs. The proportion of prescribed NSAIDS in different department of specislist are. medicine (52.68%), orthopedics (18.11%), pediatrics (13.30%) and gynocologists (7.94%) were prescribed among them 30% generic are aspirin and 50% generic contain paracetamol . in this analysis we found that the most dominating brands are ACE from square (21%),napa from baximco (18%),ecospirin from acme (17%) and diclofenac from opsonin(16%) cover the market.The prescribers did not follow the WHO core prescribing indicators well (as 46% did not follow EDL list) and deviated from good prescribing practices.

Keywords: NSAIDs, Multivitamins, Rational use, prescribing pattern, Medical practitioners; prescription quality; Rational drug use; WHO prescribing indicators.

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Chapter-I

Introduction

1.1 Introduction:

Bangladesh is one of the most densely populated countries in the world. It is a unitary state and parliamentary democracy. Health and education levels are relatively low, although they have improved recently as poverty levels have decreased. Bangladesh faces a number of major challenges, including poverty, corruption, overpopulation and vulnerability to climate change. However, it has been lauded by the international community for its progress on the Human Development Index. Bangladesh has made more notable gains in a number of indicators than some of its neighbors with higher per capital income, such as India and Pakistan. The joint donor funded Health, Population, and Nutrition Sector Development Programme (HPNSDP) has contributed to significant improvement in a number of health indicators including reduction in under-five mortality, immunization coverage, maternal mortality and total fertility. Despite current economic growth, poverty and income inequality remain persistent challenges in Bangladesh. Simultaneous with the demographic transition, Bangladesh is undergoing the health transition and manifesting the double burden of disease attributable to the emergence of noncommunicable diseases. The health system of Bangladesh is a pluralistic system with some key actors that define the structure and function of the system (Vaughan, Karim and Buse, 2000).

1.1.1 Health care system in Bangladesh

The Health care system in Bangladesh falls under the control of the Ministry of Health and Family Planning. The government is responsible for building health facilities in urban and rural areas. For example, in the late 1980's in Bangladesh, the rural health facilities that existed in the rural areas were mostly sub-district health centers, rural dispensaries and family welfare centers. Unfortunately, they were poorly administered (WHO, 2010).

In Bangladesh, the majority of the country's population lives in rural areas, while the majority of health professionals work in urban centers. Also, the rapid growth of the private medical system meant that fewer professionals remained in the public sector to take care of the masses. Private systems are mostly out of reach for poor people who can barely afford to live day by day.

The health system in Bangladesh is supply-side financed, meaning that poor households can have access to medical treatments or at least to essential medical care. Still, there is a large gap because community financing programs are missing (WHO, 2010).

1.1.2 Medicine and its use in the healthcare system:

To ensure rational and appropriate use of drugs in Bangladesh was another prime concern . But there has been no drug use study in the country . Clinically inappropriate and inefficient use of medicines is a serious problem. More than half the medicines in Bangladesh are inappropriately prescribed, dispensed or sold. Despite legal prohibitions , numerous drugs with similar or no significant benefits are available in the market. As a specific example, there are seven members of the angiotensin-converting enzyme (ACE) inhibitors available in the country. The efficacies and chemical structures of these molecules are more or less similar, but their price vary significantly . The drug policy clearly prohibits the production of multi-ingredient preparations of vitamins and minerals with the exception of B-complex vitamins. But a mixture of 32 vitamins and minerals including selenium, vanadium, molybdenum, tin and many other unnecessary ingredients has been marketed in the country for a few years, violating the principles of the NDP. The need for these trace elements in Bangladesh is not established whereas nutritional deficiencies are mainly related to vitamins A and B-complex, iron, calcium, iodine and zinc. Irrational prescription and use of antibiotics are rampant throughout the country, with an estimated half of all antibiotics being sold without prescriptions . Self-medication is widespread, and all types of medicines can be purchased without a prescription . There are about 30,000 illegal and 80,000 unlicensed drug stores operating in the country. It is alleged that both legal and illegal drug dealers are engaged in selling fake, smuggled and adulterated medicines in the country (Issuesinmedicalethics.org, 2016)

1.2 Supply of the medicine

Before Liberation, there was hardly any pharmaceutical enterprise in Bangladesh (then East Pakistan). After several years of liberation, the government could not increase (in relative terms)

budgetary allocations for the improvement of health sector. At that time, most of the people had little access to the essential lifesaving medicines. This sector started to improve from 1980s. The pharmaceutical industry has grown in the last two decades at a considerable rate.

1.3 Pharmaceutical Industry of Bangladesh

The pharmaceutical industry in Bangladesh is one of the most developed hi-tech sectors within the country's economy. In 2000, there were 210 licensed allopathic drug-manufacturing units in the country, out of which only 173 were in active production; others were either closed down on their own or suspended by the licensing authority for drugs due to non-compliance to good manufacturing practices or drug laws. Now about 300 pharmaceutical companies are operating at the moment. The industry manufactured about 5,600 brands of medicines in different dosage forms. There were, however, 1,495 wholesale drug license holders and about 37,700 retail drug license holders in Bangladesh (Dspace.bracu.ac.bd, 2016).

Here are the names of the pharmaceutical companies of Bangladesh:

- Square Pharmaceuticals
- Incepta Pharmaceuticals
- Beximco Pharmaceuticals
- Oponin Pharma
- Renata
- Eskayef Bangladesh
- ACI
- Acme Pharmaceutical
- Aristopharma
- Drug International
- Sanofi-Aventis Bangladesh Ltd
- GlaxoSmithKline(GSK) Bangladesh Limited
- Orion Pharma Ltd
- Novo Nordisk

- Healthcare Pharmaceuticals Limited
- General Pharmaceuticals Ltd
- Sandoz (generic pharmaceuticals division of Novartis)
- Popular Pharmaceuticals Ltd. (PPL)
- Novartis (Bangladesh) Limited
- IBN SINA Pharmaceutical Industry Ltd. (IPI)
- Nuvista Pharma Limited
- UniMed UniHealth Pharma Ltd
- Sun Pharmaceutical (Bangladesh) Ltd
- Globe Pharmaceuticals Ltd
- BIOPHARMA Ltd
- Roche Bangladesh Ltd
- Radiant Pharmaceuticals Ltd
- Pacific Pharmaceuticals Ltd
- Jayson Pharmaceuticals Ltd
- BEACON Pharmaceutical Limited
- Social Marketing Company (SMC)
- Orion Infusion Ltd
- Kemiko Pharmaceuticals Ltd
- NAVANA Pharmaceuticals Ltd
- Delta Pharma Ltd
- Servier Bangladesh
- SOMATEC Pharmaceuticals Ltd
- Rangs Pharmaceuticals Ltd
- Libra Pharmaceuticals Ltd
- ALCO Pharma Ltd
- Apex Pharma Ltd
- Pharmadesh Laboratories Ltd
- Silva Pharmaceuticals Ltd
- Medimpex Bangladesh
- Edruc Limited

- Ziska Pharmaceuticals Ltd
- White Horse Pharmaceuticals
- RAK Pharmaceuticals Pvt. Ltd
- Asiatic Laboratories Ltd (Dspace.bracu.ac.bd, 2016).

1.4 Market Flashback:

pharmaceutical is now one of the fastest growing sectors. In 2013, the total size of the pharmaceutical market of Bangladesh was estimated to be approximate Tk. 101 Billion. With an annual growth rate of about 8.12 %, Bangladesh Pharmaceutical Industry is now selfsufficient in meeting the local demand.

According to IMS Report of 4th quarter of 2013 the current local pharmaceutical market scenario of Bangladesh is as follows:

- Total Market: 101,685,403,612 BDT
- Annual Growth: 8.12%

Here is a view of top ten pharmaceutical companies of Bangladesh with their market share and growth:

Square Pharmaceuticals retained the top position with its local sales figure reaching Tk 19.72 billion in 2013 in the country's Tk 101 billion pharmaceutical market followed by Incepta Pharmaceuticals. Its total sales were Tk 10 billion in 2013. Beximco Pharma's position in the country's top 10 pharmaceutical companies was the third in terms of sales. Fourth position took by the Opsonin Pharma Ltd., established in 1956. Renata took the fifth position. Sanofi-Aventis ranked the second among the multinational pharmaceutical companies followed by GlaxoSmithKline.

In Bangladesh there has been huge demand for PPIs, antibiotics and anti-pyretics. Thus these drugs comprise the top ten pharmaceutical products for the country. The recent IMS data exhibits the top ten medicines for Bangladeshi market.

The top ten pharmaceutical brands of Bangladesh are:

Table: Top Ten Brands (December, 2013; IMS)

Si. No. Brand Name Drug Class Name of the Company

Growth (%)

1 Seclo Proton Pump Inhibitor

Square 35.05

2 Losectil Proton Pump Inhibitor

Eskayef -6.43

3 Maxpro Proton Pump Inhibitor

Renata 22.41

4 Pantonix Proton Pump Inhibitor

Incepta 13.11

5 Cef-3 Antibiotic

Square 13.92

6 Napa Anti-pyretic

Beximco 4.34

7 Neotack Anti-ulcerant

Square 3.58

8 Napa Extra Anti-pyretic

Beximco 12.04

9 Serigel

Health Care 28.73

10 Zimax Antibiotic

Square -4.22 (Dspace.bracu.ac.bd, 2016).

1.5 Pharma market and their marketing strategy in Bangladesh

The pharmaceutical market in Bangladesh is highly concentrated (top ten control around 70 % of the market). Due to high competition aggressive marketing strategies are adopted for greater market share, which sometimes cross limit. There is lack of data on this aspect in Bangladesh. This exploratory study aimed to fill this gap by investigating current promotional practices of the pharmaceutical companies including the role of their medical representatives (MR). This qualitative study was conducted as part of a larger study to explore the status of governance in health sector in 2009. Data were collected from Dhaka, Chittagong and Bogra districts through in-depth interview (healthcare providers and MRs), observation (physician-MR interaction), and round table discussion (chief executives and top management of the pharmaceutical companies). Findings reveal a highly structured system geared to generate prescriptions and ensure market share instituted by the pharmaceuticals. A comprehensive training curriculum for the MRs prepares the newly recruited science graduates for generating enough prescriptions by catering to the identified needs and demands of the physicians expressed or otherwise, and thus grab higher market-share for the companies they represent. Approaches such as inducements, persuasion, emotional blackmail, serving family members, etc. are used. The type, quantity and quality of inducements offered to the physicians depend upon his/her capacity to produce prescriptions. The popular physicians are cultivated meticulously by the MRs to establish brand loyalty and fulfill individual and company targets. The physicians, willingly or unwillingly, become part of the system with few exceptions. Neither the regulatory authority nor the professional or consumer rights bodies has any role to control or rectify the process. This study was done as part of a larger study by Bangladesh Health Watch 2009 which explored issues related to governance in the health sector including the pharmaceutical sector. It aimed to investigate the extent of

ethical procedures followed in the marketing practices of the pharmaceutical companies and the role of their MRs in this process. Findings reveal a structured and evidence-based drug promotion strategy instituted by the pharmaceutical companies which frequently violates ethics (Mohiuddin *et al.*, 2015).

The need for NDP was very evident. Almost all the multinational companies were producing simple and non-essential drugs in Bangladesh like vitamins mixture or cough syrups.

There was a need for vast quantity of essential, useful and economic drugs in Bangladesh. It was essential and important for Bangladesh to introduce a drug policy for the betterment of national health by availing international standard medicine in lower cost to Bangladeshi people. Precisely, multinational companies were prevented to reduce their unessential drugs production and discouraged to import raw material at high process (Dspace.bracu.ac.bd, 2016).

1.6 National drug policy

THE OBJECTIVES OF A NATIONAL DRUG POLICY World Health Organization (WHO) points out three objectives as crucial of a national drug policy. These are: 1. Access: equitable availability and affordability of “essential medicine“ including traditional medicines. 2. Quality: the quality, safety and efficacy of all medicines. 3. Rational use: implies promotion of therapeutically sound and cost-effective use of medicine by health professionals and consumers. This paper discusses these objectives from Bangladesh perspective.

(A) PRICE LIMITATION:

At present in Bangladesh there are one hundred and seventeen (117) essential medicines, the prices of which are fixed by the drug administration. In case of others, company price is endorsed by the administration. However, the real situation does not reflect the principle of price fixation. One or two example is enough to prove this. “Ciprofloxacin” is a life saving antibiotic and vastly used for many diseases. Even at present, cost of Ciprofloxacin extends from Tks 5 to 14, a price variation of 180%.⁴ It is very difficult to explain this variation in price. Whether the cheaper one is made at low cost sacrificing the quality and its reverse is also true.

(B) QUALITY, SAFETY AND EFFICACY:

Still there is no adequate drug testing facility in Bangladesh. Presently, drug administration has a laboratory but it is quite inadequate for the total demand. We know that as a developing country, so we have many limitations..

(C) USEFULNESS AND RATIONAL USE:

The physicians are the ultimate judges in this regard. According to our 1982 drug policy, there is a clear indication that no company can market a drug of similar benefits as of the existing one with minor chemical difference. but many companies are not abide by the act. So the whole society is exposed to unnecessary drug with potential risk. For an example, in case of cardiovascular disease, use of angiotensin converting enzyme inhibitor is very popular. At present, in Bangladesh, there are captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, and ramipril in use.⁴ Of course, the efficacy of captopril and the related progeny is more or less same, but the price varies from 3 taka (approx. 2 Pak. rupees) per tablet to 18 taka (approx. 12 Pak. rupees) per tablet is another example of the same class of agents. This corresponds to a variation of 500%! So every physician should use cost-effective drug. But many physicians are using others instead of captopril, possibly because of personal illegal interest and unethical, aggressive promotional activity of the pharmaceutical companies (Chowdhury, Bari and Khan, 2012).

1.6.1 DGDA and other authorities

The Bangladesh Association of Pharmaceutical Industries – BAPI: BAPI, (Bangladesh Aushad Shilpa Samity in Bengali), established in 1972 with just 33 members, has been playing a very vital role for development of this sector. Today, BAPI is a very strong organization having as many as 144 companies as its members.

Drug Regulatory Authorities in Bangladesh A regulatory agency is a public authority or government agency responsible for exercising autonomous authority over some area of human activity in a regulatory or supervisory capacity. An independent regulatory agency is a regulatory agency that is independent from other branches or arms of the government. Two organizations regulate drugs and pharmacies in Bangladesh, one governmental and one semi-government,

which are: The Directorate General of Drug Administration (DGDA) The Pharmacy Council of Bangladesh (PCB)

The Directorate General of Drug Administration (DGDA): DGDA is the drug regulatory authority of Bangladesh, which is under the Ministry of Health and Family Welfare. DGDA regulates all activities related to import and export of raw materials, packaging materials, production, sale, pricing, licensing, registration, etc. of all kinds of medicine including those of Ayurvedic, Unani, and Herbal and Homoeopathic systems.

The Pharmacy Council of Bangladesh (PCB): PCB was established under the Pharmacy Ordinance in 1976 to control pharmacy practice in Bangladesh.

The Bangladesh Pharmaceutical Society is affiliated with international organizations International Pharmaceutical Federation and Commonwealth Pharmaceutical Association. The National Drug Policy (2005) states that the WHO's current Good Manufacturing Practices (GMP) should be strictly followed.

1.7 Prescribing Pattern of the doctors in the healthcare system of Bangladesh

Irrational prescribing of medicines is a global problem, particularly in developing and transitional countries. Country like Bangladesh, irrational prescribing is common finding. Frequently observed irrational use of medicine includes the use of too many medicines per patient (poly-pharmacy), inappropriate use of antimicrobials, over use of injections and vitamins. On the other hand, aggressive drug marketing, lack of information on the use of drug and inadequate drug supply has been suggested to be the main causes behind the irrational prescribing. Irrational drug use leads to reduction in the quality of drug therapy, wastage of resources, increased treatment costs, increased risk for adverse drug reactions and emergence of drug resistance. The high cost of prescribed drug causes problems in developing countries like Bangladesh (Begum *et al.*, 2013).

The quality of prescribing is a major determinant of how patients use medicines. It plays a crucial role in the treatment of serious health conditions when people do tend to consult health

professionals. The way in which health professionals prescribe multiple medicines reinforces consumers beliefs that they need “a pill for every illness” and that a cure is unlikely without using medicines. It also affects the treatment of less severe conditions as people tend to remember the advice given and use it in later episodes of self-medication.

All over the world, 50% of medications are prescribed inappropriately, and further, 50% of these are used inappropriately.⁴ Common irrational uses of drugs include over- or underuse of medications, high cost of the medications, indiscriminate and frequent use of injections and antibiotics, use of multiple medications, use of brand instead of generic names in prescribing, and prescribing medications not in accordance to a standard treatment guidelines or not from EDL are major problems of present-day medical practice. (Summoro *et al.*, 2015)

1.7.1 Standard prescribing indicators:

World health organization (WHO) has designed standardized prescribing indicators to evaluate the trends of prescribing in health facilities. These are the number of drugs per encounter, the percentage of drugs prescribed by brand name, the percentage of antibiotics and injectable drugs per encounter, and the percentage of drugs prescribed from an essential drug list (EDL). These indicators are used to describe current treatment practices, compare health facilities and prescribers, and allow for identification of potential drug-use problems that may affect patient care.^{1–3} The WHO recommended value of the number of medicines per prescription ranges from 1.4 to 1.8, antibiotics prescription 20% to 27%, and injectable medicines 13.4% to 24.1%, whereas standard accepted value for prescribing by generic name and from EDL is 100%. Based on these recommended values, drug-prescribing patterns in health institutions can be evaluated. Hence, based on an evaluation, the necessary modification to the pattern to achieve rational and cost-effective medication use may be suggested. A minimum of 600 patient records can be evaluated retrospectively for drug-prescribing pattern study in health facilities (Summoro *et al.*, 2015).

1.7.2 Prescribing by generic name

Writing prescriptions using generic name is an important drug-use quality to avoid undesirable drug interactions, adverse drug reactions, and medication errors. The average percentage of drugs prescribed by generic name in the four hospitals was 95.8. DSMGH and TZH exhibited the acceptable values in terms of the WHO criteria with regard to prescribing by generic names (almost 100%), whereas it was found to be lower in country. Private pharmacies might have influenced the prescribing patterns in later cases as they are relatively located in main city where there are alternative private pharmacies, whereas the former are located in small towns. This can be explained by a reason given by a doctor for a question, “why not all drugs are prescribed by generic name?” which was answered as “Some physicians who are working as part-time in private health facilities are more familiar with brand name than generic name”. But generally, in light of other local and international studies and according to the judgment criteria, the use of generic names in the hospitals in this study may be judged as a very good performance. For example, the study of southwest Ethiopia¹² revealed that 92% of the drugs were prescribed by generic names, whereas those in Sudan¹⁵ and India¹⁶ indicated that only 43.6% and 73.4% of drugs were prescribed by generic name, respectively (Summoro *et al.*, 2015).

1.7.3 Prescribing from EDL

Rational drug use is achieved when there is rational prescribing using medicines from an EDL. Identifying a limited number of essential medicines leads to a better supply, more rational use, and lower costs. Drugs in the EDL are intended to fulfill the real needs of the majority of the population in diagnostic, prophylactic, therapeutic, and rehabilitative services using criteria such as risk–benefit ratio, cost-effectiveness, quality, practical administration, patient compliance, and acceptance (Summoro *et al.*, 2015).

1.7.4 LIST OF SOME ESSENTIAL DRUGS

Sl. Name of drugs Dosage form

- > Acetazolamide Tablet
- > Aciclovir Powder for injection, Tablet
- > Allopurinol Tablet
- > Aluminium hydroxide + Magnesium hydroxide Oral liquid, Tablet
- > Amitriptyline Tablet
- > Benzathine benzylpenicillin Powder for injection
- > Benzoic acid + Salicylic acid Ointment or cream
- > Benzyl penicillin Powder for injection
- > Betamethasone Ointment or cream
- > Bleomycin Powder for injection
- > Bupivacaine Injection
- > Calcium gluconate Injection
- > Carbamazepine Oral liquid, Tablet (chewable), Tablet (scored)
- > Chloramphenicol Eye drops, Eye ointment
- > Chloroquine Oral liquid, Tablet
- > Chlorpheniramine Injection , Tablet
- > Ferrous salt Oral liquid, Tablet
- > Ferrous salt + Folic acid Capsule, Tablet

- > Folic acid Tablet
- > Furosemide Injection, Tablet
- >Gentamycin Injection, Solution (eye drops)
- > Gentamycin + Hydrocortisone Ear drop
- > Haloperidol Injection, Tablet
- > Halothane Inhalation
- > Hepatitis B vaccine Injection
- > Ibuprofen Tablet
- > Insulin Injection (Soluble) Injection
- > Isoniazide Tablet, Tablet (scored)
- > Levodopa + Carbidopa Tablet
- > Metformin Tablet
- > Methotrexate Powder for injection, Tablet
- > Methyldopa Tablet : 250 mg
- > Neostigmine Injection, Tablet
- > Nevirapine (NVP) Oral liquid, Tablet
- > Omeprazole Capsule
- >Paracetamol Oral liquid, Suppository, Tablet
- > Procainamide
- > Vitamin B-Complex (Vitamin B1- 5 mg + Vitamin B2- 2 mg + Vitamin B6 - 2 mg + Nicotinamide 20 mg) (Anon, 2016).

1.8 NSAIDS:

Non-steroidal Anti-inflammatory Drugs (NSAID), are among the most widely used and misused of all drugs. Though they provide symptomatic relief from pain and swelling in chronic joint diseases, they may cause renal impairment, especially in combination with other nephrotoxic agents. Nonsteroidal anti-inflammatory drugs (NSAIDs) represent diverse group of drug with analgesic property and most frequently prescribed drug globally. This is first choice of drug with well demonstrated efficiency for the pain management primarily musculoskeletal disorder and osteoarthritis to treat mild to moderate pain. Although its serious toxicity related to GIT limits its expediency. "Big evil" have tendency to just cure pain relieving symptoms not disease (Journal of Scientific and Innovative Research 2014).

1.8.1 NSAIDs and their Mode of Action:

Prostaglandins are a family of chemicals that are produced by the cells of the body and have several important functions. They promote inflammation that is necessary for healing, but also results in pain, and fever support the blood clotting function of platelets; and protect the lining of the stomach from the damaging effects of acid.

Prostaglandins are produced within the body's cells by the enzyme cyclooxygenase (COX). There are two COX enzymes, COX-1 and COX-2. Both enzymes produce prostaglandins that promote inflammation, pain and fever. However, only COX-1 produces prostaglandins that support platelets and protect the stomach. Non steroidal anti-inflammatory drugs (NSAIDs) block the COX enzymes and reduce prostaglandins throughout the body. As a consequence, ongoing inflammation, pain, and fever are reduced. Since the prostaglandins that protect the stomach and support platelets and blood clotting also are reduced, NSAIDs can cause ulcers in the stomach and promote bleeding (Omudhome Ogbu, 2016).

1.8.2 Pharmacologic Effects

All NSAIDs, except for acetaminophen (also named paracetamol), are antipyretic, analgesic, and anti-inflammatory. The use of NSAIDs for the relief of pain in companion is standard practice. In general, NSAIDs provide only symptomatic relief from pain and inflammation and do not significantly alter the course of pathologic damage. As analgesics, they are generally less effective than opioids and are therefore generally indicated only against mild to moderate pain in people. However, NSAIDs also find use in management of severe pain, optimally in combination with an opioid.

1.8.3 Administration and Pharmacokinetics

Most NSAIDs are weak organic acids that are well absorbed after oral administration. However, food can impair the oral absorption of some NSAIDs (eg, phenylbutazone, meclofenamate, flunixin, and robenacoxib). Several NSAIDs are available as parenteral formulations for IV, IM, or SC administration. Some parenteral formulations are highly alkaline (eg, phenylbutazone) and may cause tissue necrosis if injected perivascularly. Once absorbed, most NSAIDs are extensively (up to 99%) bound to plasma proteins, with only a small proportion of unbound drug available to be active in the tissues. NSAIDs may also compete for binding sites with other highly protein-bound compounds, leading to some drug displacement; however, this displacement has little therapeutic consequence because it does not affect the concentration of the free drug. Because NSAIDs are highly protein bound and extravasation of protein occurs in inflammation, NSAIDs tend to concentrate in areas of inflammation. Consequently, their duration of action typically exceeds that predicted by elimination half-life.

Most NSAIDs are biotransformed in the liver to inactive metabolites that are excreted either by the kidney via glomerular filtration and tubular secretion or by the bile. Mavacoxib is an exception, mostly being excreted unchanged in the bile. Some NSAIDs, including naproxen, etodolac, and meclofenamic acid, undergo extensive enterohepatic recirculation in some species, resulting in prolonged elimination half-lives.

1.8.4 Indication of NSAIDs:

Common acute (short-term) conditions that can be treated with NSAIDs include:

- headaches
- painful periods
- toothache
- soft tissue injuries such as sprains and strains
- infections, such as the common cold or the flu (NSAIDs do not treat the underlying infections, but can help to relieve symptoms; especially fever)

Common chronic (long-term) conditions that can be treated with NSAIDs include:

- most types of arthritis, including rheumatoid arthritis, other forms of inflammatory arthritis and osteoarthritis
- chronic back pain
- chronic neck pain (Nhs.uk,2014)

1.8.5 Necessities of NSAIDS in different illness:

Diseases	First choice	Alternatives
Inflammation and Rheumatic Diseases	Celecoxib	None
Inflammation and Rheumatic Diseases	Diclofenac	None
Osteoarthritis ,Rheumatoid arthritis	Diflunisal	None
Inflammation and Rheumatic Diseases	Etodolac	None
Rheumatoid arthritis, osteoarthritis	Fenoprofen	None
Osteoarthritis ,Rheumatoid arthritis	Flurbiprofen	None
Inflammation and Rheumatic Diseases	Ibuprofen	None
Inflammation and Rheumatic Diseases	Indomethacin	None
Inflammation and Rheumatic Diseases	Ketoprofen	None
post operative pain	Ketorolac tromethamine	None (Bpac.org.nz, 2016).

1.8.6 Adverse Effects

All NSAIDs have the potential to induce adverse reactions, some of which can be life threatening. Many reactions to NSAIDs are dose-related and are typically reversible with discontinuation of therapy and supportive care.

Vomiting is the most common adverse effect. GI ulceration is the most common life-threatening adverse effect. Loss of GI protective mechanisms results from inhibition of constitutive prostaglandins that regulate blood flow to the gastric mucosa and stimulate bicarbonate and mucus production. This disrupts the alkaline protective barrier of the gut, allowing diffusion of gastric acid back into the mucosa, injuring cells and blood vessels and causing gastritis and ulceration. As organic acids, NSAIDs, especially aspirin, may also cause direct chemical irritation of the GI mucosa. The enterohepatic recirculation of certain NSAIDs may result in high biliary concentrations that increase ulcerogenic potential in the gut. NSAID-induced GI bleeding may occur leading to iron-deficiency anemia, or be more severe, resulting in vomiting, hematemesis, and melena.

GI blood loss may be further complicated by impaired platelet function; NSAIDs, by inhibiting COX-1, prevent platelets from forming TXA₂, a potent aggregating agent. Because TXA₂ inhibition causes prolonged bleeding.

Nephropathies associated with chronic NSAID use are common in people. It is important to maintain hydration and renal perfusion in people receiving NSAIDs, especially those undergoing anesthesia or surgery.

Hepatopathies are relatively common in people receiving NSAIDs. NSAID administration routinely induces mild hepatic changes characterized primarily by increases in liver enzymes without clinical signs or hepatic dysfunction. Rare reports of idiosyncratic reactions resulting in hepatic dysfunction or failure have been reported in people (acetaminophen and others), Cytopathic (hepatocellular injury, necrosis), cholestatic, and mixed histopathologic patterns of injury have been documented. NSAIDs should be used with caution in people with preexisting hepatic disease (Merckvetmanual 2016).

1.8.7 Drug interaction of NSAIDs

NSAIDs reduce blood flow to the kidneys and therefore reduce the action of diuretics ("water pills") and decrease the elimination of lithium (Eskalit Lithobid) and methotrexat (Rheumatrex, Trexall). As a result, the blood levels of these drugs may increase as may their side effects.

NSAIDs also decrease the ability of the blood to clot and therefore increase bleeding. When used with other drugs that also increase bleeding (for example, warfarin [Coumadin]), there is an increased likelihood of serious bleeding or complications of bleeding. Therefore, individuals who are taking drugs that reduce the ability of blood to clot should avoid prolonged use of NSAIDs.

Persons who have more than three alcoholic beverages per day may be at increased risk of developing stomach ulcer. (Omudhome Ogbu, 2016).

1.8.8 Risk Factors for NSAID-Induced Gastrointestinal Adverse Events

It should be noted that the risk for serious gastrointestinal complications increases in the following patient groups, necessitating prudent drug choice:

- patients over the age of 65,
- patients with a history of previous peptic ulcer disease,
- patients taking corticosteroids,
- patients taking anticoagulants,
- patients taking aspirin.

A recent meta-analysis of 18 case-control and cohort studies published between 1990 and 1999 identified age and previous peptic ulcer disease, particularly if complicated, as the strongest predictors of absolute risk.

1.8.9 CURRENT RECOMMENDATIONS FOR THE USE OF NSAIDS

A The evidence for the gastrointestinal and cardiovascular adverse effects of NSAIDs have substantial implications for public health, patient education and therapeutic decision making on the part of physicians charged with managing pain-related conditions. A few organizations have published guidelines on the use of NSAIDs and COX-2 inhibitors. Generally, any recommendations should offer effective pain control along with optimal gastro protection, together with an assessment of cardiovascular and gastrointestinal risks before initiation of NSAIDs or COX-2 inhibitors therapy.

The Food and Drug Administration expert advisory committee recommends that:

- When COX-2 inhibitors and NSAIDs are to be used for the management of individual patients, they should be prescribed with the lowest effective dose and for the shortest duration.
- They should not be prescribed for high risk patients, e.g., patients with a history of ischemic heart disease, stroke or congestive heart failure, or in patients who have recently undergone CABG.
- All prescription-strength NSAIDs will now display “black box” label warnings for the potential risk of cardiovascular and gastrointestinal adverse effects.
- Treatment with NSAIDs alone in patients aged less than 65 years who do not have gastrointestinal risk factors is considered appropriate. Co-therapy with a PPI or treatment with a COX-2 inhibitor was considered unnecessary in these patients.
- The use of a NSAID alone was considered inappropriate in any patient with a previous gastrointestinal event and in those who concurrently receive aspirin, steroids or warfarin. These patients should receive either a NSAID plus a PPI or a COX-2 inhibitor.
- Use of a COX-2 inhibitor with PPI co-therapy is appropriate only in patients at very high risk, such as those with a previous gastrointestinal event who are taking aspirin, and those who are taking aspirin plus steroids or warfarin (Ong *et al.*, 2007)

1.9 Multivitamins

The physicians have been prescribing vitamins for different reasons since hundred years. Since 1982, only few vitamin preparations were available in Bangladesh, of which majority were single ingredient preparations . People were being satisfactorily treated with those vitamins. Though information relating role of multivitamins in disease prevention is weaker than the individual vitamins . multivitamin prescribing has become popular since its availability . Bangladesh is neither an exception, the consumption of vitamin has increased recently in Bangladesh , which perhaps resulted as consequence of entry of multivitamin into the market . The growth of vitamin market is difficult to rationalize only on the basis of nutritional status of the people, as there was no sudden change in that situation.

1.9.1 Indication of multivitamin

For certain people, particularly the elderly, supplementing the diet with additional vitamins and minerals can have health impacts, however the majority will not benefit. People with dietary imbalances may include those on restrictive diets and those who cannot or will not eat a nutritious diet. Pregnant women and elderly adults have different nutritional needs than other adults, and a multivitamin may be indicated by a physician. Generally, medical advice is to avoid multivitamins, particularly those containing vitamin A, during pregnancy unless they are recommended by a health care professional (Formulary Journal, 2016).

1.9.2 Use of multivitamins in our country

In Bangladesh, people usually take thiamin and niacin more than their daily requirements, though riboflavin and vitamin C deficiency were observed in few people . In deficiency of specific vitamin, that particular vitamin might be prescribed in individual cases . However, vitamin prescribing has increased significantly without confirmation of specific deficiency or evidence of lack of specific vitamin in the diets of the people . Prescribing of vitamins in this

manner offers little or no benefit to the recipients, rather causes excessive intake of prescribed vitamins, which might even become harmful. Different studies revealed controversial facts about the status of vitamin use in clinical medicine (Das and Rahman, 2010).

1.9.3 Impact of multivitamin as combination therapy

Irrational Drug Combinations or Fixed Dose Combinations (FDCs) are combinations of two or more active drugs in a single form. The rationality of a fixed dose combination is the most controversial and debated issue in today's clinical practice. Combination drugs increase the risk of side effects, lead to an ineffective dosage and liability to abuse and may also needlessly increase the cost. Drug combinations make it more difficult to find the causative agent responsible for the adverse reactions. In many cases their stability is doubtful, reducing the efficacy of many preparations. The Fifteenth WHO model list of essential medicines contains only 25 approved fixed dose combinations, whereas in some countries, there are innumerable examples of irrational drug combinations, which are easily available and can be bought even without a prescription. A system of screening the drug combinations that are already licensed and available in the market is implemented in many developed and developing countries. Vitamin and mineral supplements are used up to (54%) by self medication in chronic fatigue syndromes, anemia, lethargy and strangely even in weight loss as reported by few during our study. They are generally believed to be safe and are used for chronic time periods. Whereas, over dosage and misuse of vitamins is reported to cause toxicities and complication (International Journal of Experimental Pharmacology, 2016).

1.9.4 Mixture of multivitamin or minerals and its necessity

Recently, different companies in our market launched a mixture of vitamins and mineral. But is there any justification of marketing this sort of drug in a country like Bangladesh? What are the deficiency diseases we commonly found in Bangladesh in our common practice? Most are due to Vitamin A or B complex, iron, calcium, iodine, or zinc deficiency. B-Complex or multivitamin

preparation and/or specific mineral replacement is enough to treat these cases. There are very seldom diagnoses of selenium or vanadium deficiency or molybdenum deficiency, if ever. How many amount of tin are required for a healthy life? So, there is no point in prescribing these type of agents to our poor people. Because a single tablet costs about 6-7 taka (approx. 4-5 Pak. rupees), whereas common multivitamin takes only 1-1.5 taka (less than 1 Pak. rupees/tablet. This type of vitamin-mineral mixture is still absent in the market of Britain, Australia, New Zealand and other European countries. British pharmacopoeia clearly indicates that there is no justification for prescribing multiple ingredient vitamin preparation. Even according to our 1982 drug policy, this is completely unlawful because a mixture of vitamin and mineral has no proven scientific basis. (Chowdhury, Bari and Khan, 2012)

1.9.5 Rational use of multivitamins

The most common supplements are multivitamins that typically include the RDA of thiamin, riboflavin, niacin, folic acid, and vitamins A, C, B6, B12, D, K, and E. Few studies have evaluated the effects of multivitamins percentage rather than specific components of them. In prospective studies, the daily use of a multivitamin has been associated with a lower risk of coronary disease, colon cancer and breast cancer. This is more so for patients consuming alcohol. In elderly persons, a multivitamin –multi mineral combination reduced the number of days of illness due to infections by half. Another study from China showed reduced incidence of stroke, primarily among men, in a nutritionally deficient population. More studies need to be done to corroborate these results. Healthy individuals do not require a daily multivitamin. There is no scientific basis for recommending vitamin -mineral supplements to the healthy population. No supplement trial has ever been able to reproduce the health benefits of eating adequate amounts of fresh fruits and vegetables.

- ✓ Pregnant and breast feeding women should take vitamin D supplements
- ✓ Women trying to conceive and women in the first 12 weeks of pregnancy should take folic acid
- ✓ People aged 65 and over should take vitamin D supplements
- ✓ People who are not exposed to much sun should take vitamin D supplements

- ✓ All children aged six months to five years should be given a supplement containing vitamins A, C and D (Stratton and Elia, 2007).

1.10 Objective of the study

The objective of this study to observe the prescribing pattern of NSAIDs among the specialist doctor in different area of Bangladesh.

In addition this study was also done to observe the adherence with the EDL to observe the mostly prescribed generic and brands of NSAIDS in our country.

1.11 Significant of the study Inadequate supply of essential drugs, substandard quality, uncontrolled drug prices and inappropriate uses of drugs are major problems in Bangladesh .There was a need for vast quantity of essential, useful and economic drugs in Bangladesh. This problem can be minimized by prescribing drugs by generic name and selection of drugs from essential medicine list. Generic drugs are substitute of branded drug without any patent protections with similar efficacy but 40 to 60% cheaper than branded drugs.

This research will bring out the list of NSAIDS drugs which are commonly prescribed by the doctors .if the out come do not show the significant adherence with the EDL then the EDL list need to be updated,

This research will bring out the list of NSAIDS generics and brands which are commonly prescribed by the doctors .if this mostly covered by few generics and few companies ,then this out come indicates the significant of aggressive marketing and irrational use of drug.,

Chapter-II

Literature Review

Literature review

2.1 Prescription practices of public and private health care providers

Irrational drug use and inappropriate prescription of drugs are major problems in developing countries, like Bangladesh and so drug use patterns need to be evaluated. Prescriptions were obtained from patients visiting private and public hospitals in rural areas of north Maharashtra, India, and analyzed. Two well trained pharmacists collected handwritten prescriptions from patients visiting community pharmacies. The prescriptions they collected were analysed for adherence with core prescribing indicators of the World Health Organization (WHO). The evaluation of prescription quality was based on the layout, legibility and clarity of the instructions in the prescriptions. The average number of drugs per prescription was 3.31, denoting poly pharmacy. The extent of prescribing drugs by generic name was strikingly low (1.5%), and the percentage of prescription of essential drugs was 52.3%. The proportion of prescriptions in which injections were listed was low, 4.8%. Gastrointestinal drugs (20.6%), multivitamins (16.8%), analgesics (16.7%) and antibiotics (14.8%) were prescribed more frequently. The legibility of prescriptions was poor, and the percentages of prescriptions in which details of diagnosis, route of administration and duration of treatment were cited were 25.4%, 9.14% and 22.6%, respectively. The patient's address (9.7%) and doctor's signature (70.6%) were present in few prescriptions. The prescribers did not follow the WHO core prescribing indicators well and deviated from good prescribing practices. Interventions are needed to improve the prescription patterns in the study area (Aanand D. Naik, 2016).

2.2 Prevalence of potentially inappropriate prescribing in an acutely ill population admitted to six European hospitals

Potentially inappropriate prescribing is common in Ireland. Data were collected from 900 consecutive older patients admitted to six university teaching hospitals (150 patients per centre) in Geneva (Switzerland), Madrid (Spain), Oostende (Belgium), Perugia (Italy), Prague (Czech Republic) and Cork (Ireland). Age, gender, comorbidity, cognitive status, prescription medicines taken before admission and baseline haematological, biochemical and electrocardiographic data were recorded. STOPP and Beers' criteria were applied to detect potentially inappropriate

medicines (PIMs). START criteria were applied to detect potentially inappropriate prescribing omissions (PPOs). Results The overall PIM prevalence rate was 51.3% using STOPP criteria, varying from 34.7% in Prague to 77.3% Geneva, and 30.4% using Beer's criteria, varying from 22.7% in Prague to 43.3% in Geneva. Using START criteria, the overall PPO prevalence rate was 59.4%, ranging from 51.3% in Cork to 72.7% in Perugia. Polypharmacy predicted the presence of PIMs using STOPP criteria [with >10 medications: odds ratio (OR) 7.22, 95% confidence interval (CI) 4.30–12.12, $p < 0.001$] and Beers' criteria (with >10 medications: OR 4.87, 95% CI 3.00–7.90, $p < 0.001$). Increasing co-morbidity (Charlson Index ≥ 2) and age ≥ 85 years significantly predicted PPOs. Potentially inappropriate drug prescribing and the omission of beneficial drugs are highly prevalent in acutely ill hospitalized in six European centres (Gallagher *et al.*, 2011).

2.4 Prescribing Practice for Geriatric Patients in Selected Hospitals

Due to the improvement of medical facility the elderly population in Bangladesh continues to rise. Management of many acute and chronic disease for the aging population have contributed to wide-range medication use among aged patients, these circumstances may lead to drug related problem (DRPs) especially unnecessary drug therapy. this study was to identify unnecessary drug therapy on outdoor geriatric patients and to investigate whether poly pharmacy is a suitable indicator for occurrence of redundant or irrational drug therapy in a hospital outdoor patients. Research type was cross-sectional. Data taken through preformed questionnaire among outdoor geriatric patients. The study was conducted with inclusion criteria: patient with 60 year and above. Total of 120 patients were under study during a 7-month period from February, 2013 to August, 2013. An average of 4.30 drugs was prescribed. 50% of the drugs were prescribed by generic name & 50% in brand name. Polypharmacy was observed in 35.83% of total patients. The maximum number of 12 prescribed drugs are received by 0.84% patients. Among the total patients 6.66% patients receive single drug. 30% of patients received 5-7 medicine & 5% of patients received 8-10 drugs. About 24.16% were prescribed antibiotics and 10.19% of total drug was combination of calcium carbonate and vitamin D. Most of the geriatric patients (89.16%) were counseled for more than 5 minutes. Prevention of redundant drug therapy problem can be conducted through promoting the rational use of drug This study exposes the prescription trends, and indicates possible areas of improvement in prescribing practice (Khandoker, 2013).

2.5 Drug Prescription Pattern in a Nigerian Tertiary Hospital

To evaluate the prescribing pattern of clinicians in the general outpatient unit of the Aminu Kano Teaching Hospital, Kano (AKTH), This was a descriptive retrospective study conducted using 500 prescriptions made at the general outpatient unit of AKTH between April and July 2009. Results: A total of 497 prescriptions were successfully analyzed. The average number of drugs per encounter in the facility was 3.04. Generic prescribing was low at 42.7 % while antibiotic prescription was high at 34.4 %. Injections were prescribed in 4 % of encounters while 36.2, 19.1, 25.8 and 1 % of encounters had analgesics, antimalarials, antihypertensives and anxiolytics prescribed, respectively. Vitamins were prescribed in 9.7 % of encounters. Polypharmacy, low rate of generic prescriptions and overuse of antibiotics still remain a problem in health care facilities in Nigeria.. This calls for sustained interventional strategies and periodic audit at all levels of health care to avoid the negative consequences of inappropriate prescriptions(Nargis et al., 2015)

2.6 Prescribing pattern in a primary health center in India

Prescription is the written order of the physician which is conveyed to the patient. Rational prescription writing is a skill which should be mastered at the earliest. The present study aimed to explore the prescribing pattern of interns in a primary health center in India. A cross-sectional study was conducted for a period of 2 months (June 1 2010-July 30 2010) in a primary health center attached to a medical college in India. The main outcome measure was to assess rationality of prescribing pattern of interns was measured as per World Health Organization enlisted prescribing indicators. Data analysis was done by using descriptive and inferential statistical methods: Frequencies, percentage, and mean standard deviation. A total of 1968 drugs were prescribed in 760 prescriptions analyzed with an average of 2.58 drugs per prescription. Analgesic was the most commonly prescribed drug (25.78%) followed by antibiotics (22.1%), drugs used for gastrointestinal symptom (15.78%), multivitamins (11.84%), anti-malarials (8.35%), antihistaminics (6.25%), and hematinics (5.36%). Regarding prescribing indicators, in 435 prescriptions (22.4%), antibiotics were advised. A total of 688 (34.97%) drugs were prescribed by generic name, while the percentage of drugs prescribed from essential drug list of India was 58.47%. Injectables were prescribed in 89 prescriptions (4.49%).

The study shows that irrational prescribing practices are common among the institute. The art of rational prescribing should be taught to them by medical teachers who are adequately trained in rational drug use (Banerjee and Bhadury, 2014).

2.7 Evaluation of trends of drug-prescribing patterns based on WHO prescribing indicators at outpatient departments of four hospitals in southern Ethiopia

Rational prescribing is a primary step to ensure rational drug use. Often, half of the medicines are prescribed irrationally and half of these are even used incorrectly as the patients fail to take their medicines appropriately. The aim of this research was to evaluate drug-prescribing patterns of four hospitals in southern Ethiopia. A retrospective cross-sectional study was conducted between May 15 and June 25, 2014, to evaluate the drug-prescribing patterns based on the World Health Organization (WHO) prescribing indicators. The prescription papers, kept for the last 1 year in the outpatient departments of the four hospitals, were analyzed according to WHO guidelines. Also, prescriptions in the hospitals were analyzed to determine the most frequently prescribed drugs. All the statistical calculations were performed using SPSS[®] version 20.0 software. The average number of drugs per prescription ranges from 1.82 ± 0.90 to 2.28 ± 0.90 , whereas the percentage of use of antibiotics and injections ranged from 46.7 to 85 and 15 to 61.7, respectively. The average percentages of drugs prescribed by generic name and from the essential drugs list were 95.8 and 94.1, respectively. Anti-infective and analgesic drugs are found to be the most frequently prescribed medicines. In terms of polypharmacy, there was a slight deviation in prescribing patterns from what is acceptable according to the WHO criteria. Prescribing by generic name and from essential drug list was almost optimal. There was a significant deviation in the use of injectables in two of the four hospitals (50%), whereas their use in the other two hospitals was within the acceptable range. The use of antibiotics in all the hospitals in present study was higher than the acceptable range. Generally, it seems that there is need for improvement of the prescribing patterns in the hospitals, although this should be consolidated with further studies to link the patient diagnosis and the prescribed medications (Summoro et al., 2015).

2.8 Evaluation of Prescribing Pattern of the Private Practitioners in Bangladesh

A prescription order is a written instruction of doctors to pharmacist to supply drugs in particular form to a patient and the directions to the patients regarding the use of medicines. This study was undertaken to observe the prescribing patterns of the private practitioners in Bangladesh, 430 prescriptions were collected randomly from Dhaka city and analyzed using WHO/INRUD indicators. There were average 3.40 drugs per prescription. Drugs were prescribed in generic name only in 0.20%. About 46.31% drugs were prescribed from the Essential Drug List, only 19% of prescriptions were complete in respect to patient medication information (Sultana, Sorcar and Karmaker, 2015).

2.9 Prescribing Pattern of Non-Steroidal Anti-Inflammatory Drugs at the Out patient Department of a University Teaching Hospital in Nigeria

Non-steroidal Anti-inflammatory Drugs (NSAID), are among the most widely used and misused of all drugs. Though they provide symptomatic relief from pain and swelling in chronic joint diseases, they may cause renal impairment, especially in combination with other nephrotoxic agents. This study aimed to investigate the prescription pattern of NSAID in the Out-patient Pharmacy Department of Lagos University Teaching Hospital (LUTH), Nigeria. A total of 3800 prescriptions containing NSAIDs were analyzed for information on drug name, the number of NSAIDs per prescription, the presence of ACE inhibitors and diuretics alongside NSAIDs and NSAIDs prescribed in generic or brand name. The results showed that Aspirin was the most frequently prescribed NSAID (62.2%) and 68.4% of the NSAIDs prescriptions studied were written in generic names. The total number of drugs per prescription was in most cases 3 or greater (84.6%). There were statistically significant ($p \leq 0.05$) associations between the individual NSAID prescribed and whether they were prescribed in generics or brand names; individual NSAID prescribed and the frequency of co-prescription with an ACE inhibitor and a diuretic; types of NSAID prescribed and the cost in Naira. Though most of the prescribers complied with WHO standard in their prescriptions *vis a vis* generic prescription, avoidance of polypharmacy and avoidance of drug interactions and contraindications, there is obvious need for interventional measures or strategies to improve rational prescribing for some of the prescribers tailored towards rational prescription and use of drugs (O Awodele, 2015)

2.10 Prescribing pattern of more than one NSAID

Nonsteroidal anti-inflammatory drugs (NSAIDs) represent diverse group of drug with analgesic property and most frequently prescribed drug globally. This is first choice of drug with well demonstrated efficiency for the pain management primarily musculoskeletal disorder and osteoarthritis to treat mild to moderate pain. Although its serious toxicity related to GIT limits its expediency. For the purpose of this evaluation descriptive studies was conducted based on prescription reading and case histories of more than 200 patients to rule out prescribing habit of physicians. Prescription collected were mostly from emergency (80%) and general physicians (20%). Nearly everyone patient came with intense pain related with muscular and arthritis pain. About 69% patients were being prescribed by double NSAIDs in which acetaminophen ratio was mostly high with Diclofenac sodium (ratio of 60:35). Single practice of NSAIDs has reported just 25% but more than prescription containing multiple NSAIDs 6%. Traditional NSAIDs prescribed more frequently compared to selective NSAIDs by physician which makes patients susceptible to GIT associated toxicity. For the prophylaxis of NSAIDs associated GIT bleeding only 15% patients were coprescribe by H2 receptor blocker primarily ranitidine (15%) and PPIs (7%) and other (2%). After careful consideration about prescribing habit of NSAIDs by physician we conclude that the irrational practices prevalence have been rising dangerously which needs careful consideration by health authorities (Siddiqi *et al.*, 2002).

2.11 Prescription pattern analysis in an orthopedic hospital

There are a variety of NSAIDs available for prescription: traditional non selective (NSAIDs), and the more selective COX-2 inhibitors (Coxibs). The analgesic effects of the different NSAIDs are more or less identical; however, the Coxibs are associated with a lower risk for upper gastrointestinal side effects. Thus, the Coxibs after their introduction become an alternative to traditional NSAIDs in patients exhibiting risk for upper gastrointestinal bleeding. However, Post marketing experience unmarked various adverse cardiovascular effects. Evidences of adverse CVS events with the use of COX-2 selective inhibitors have led to their decreased use. The aim of the study was to analyze the prescribing pattern of NSAIDs in patients attending Orthopedics OPD and to correlate the use of selective COX-2 inhibitors and older conventional NSAIDs in practice and also to determine type and frequency of gastro-protective drugs used with

NSAIDs. The data was collected from the out-patient case sheets of the patients who were attending Orthopedic out-patient departments (OPDs) for a period of 6 months. NSAIDs were prescribed to 48.19% of the patients. Coxibs and Non Selective NSAIDs accounted for 1.51% and 45.71% respectively. Monotherapy was given to 14.39% and FDCs accounted for 19.29%. Diclofenac 11.77 %, was the commonest prescribed NSAID in monotherapy while Paracetamol 15.12% in FDCs. Maximum number (97.66%) of patients were co- prescribed gastro protective drugs (GPDs) commonest being Rabeprazole 12.19%. The use of Coxibs have decreased to great extent because of reports of cardiovascular adverse effects. The conventional non selective NSAIDs are generally co prescribed with gastro protective drugs (Kurth, 2003).

2.12 NSAIDs and its interaction with other drug

In a study conducted by Schnitzer and colleagues, 18,325 patients aged 50 years or older were randomly assigned to lumiracoxib 400 mg once daily, naproxen 500 mg twice daily or ibuprofen 800 mg 3 times daily for 1 year. Patients were stratified by low dose aspirin use and age. Consistent with the results of previous studies of COX-2 inhibitors, the cumulative incidence of ulcer complications was reduced by 3-fold to 4-fold among patients who received lumiracoxib compared with NSAIDs, but the reduction was smaller and did not reach statistical significance among patients who received concomitant aspirin.

Recent evidence suggests that gastrointestinal benefits may also be lost in patients who receive warfarin together with NSAIDs. In a nested case-control analysis, Battistella and colleagues quantified the gastrointestinal risk in warfarin users treated with NSAIDs or COX-2 inhibitors. During the study period, 361 (0.3%) out of 98,821 elderly patients who had received warfarin were admitted with gastrointestinal hemorrhage. These patients were 1.9-fold more likely to be receiving tNSAIDs, 1.7-fold more likely to be receiving celecoxib and 2.4-fold more likely to be taking rofecoxib than to be taking no NSAIDs before hospitalization.

Concurrent use of NSAIDs and corticosteroids may also increase gastrointestinal risk. In a population-based cohort study of 45,980 patients, Nielsen and colleagues found that there was an increased risk of gastrointestinal bleeding among patients who concurrently used NSAIDs and corticosteroids (White *et al.*, 2003).

Chapter-III

Method

3 Methodology

3.1 Aim of the Study

The objective of this study to see the prescribing pattern of NSAIDs and Multivitamins among the specialist doctor's of different areas of Bangladesh.

3.2 Selection of the area

Selecting proper area for survey is a crucial part for getting perfect data, which represent the actual condition. Our capital city Dhaka is the living place of 22 million people, as the most ancient city like other facilities, the health facilities of Dhaka are better than other cities of Bangladesh. People from all part of our country come here for the treatment of their diseases. So Dhaka was selected for my survey work. There are many govt. hospitals and hundreds of private clinics in Dhaka city. we try to go where we may get most general patient. we also collect some data from outside of the Dhaka like Kumilla, Khulna, Sylhet, Chittagong, Mymensingh, Bhola.

3.3 In this survey the prescription are collected from the following hospital:

- Al-Raji hospital, Banashree, Dhaka
- Farazi hospital, Banashree, Dhaka
- Orthopedic hospital, Mirpur Dhaka
- Kurmitola General Hospital, Cantonment, Dhaka
- Bangabandhu Sheikh Mujib Medical University (BSMMU)
- Dhaka Shishu Hospital
- National Institute of Traumatology & Orthopaedic Rehabilitation, Sher-e-Bangla Nagar, Dhaka
- Uttara Crescent Hospital
- Popular Diagnostic Centre Ltd.
- IbnSina D. Lab. & Consultation Center, Badda
- Community Based Medical College, Mymensingh
- Upazila Health Complex, Lal Mohan, Bhola.

- Chittagong medical college hospital
- kushtia medical college hospital
- Khulna medical college hospital
- Shylet medical college hospital
- Shaheed monsur ali medical college and hospital Dhaka

3.4 Duration of survey

Duration of survey was 1 year commencing from may 2015 to may 2016. To complete the survey in time, a work schedule was prepared depending on different tasks of the study. One month was spent for selection of topic, development of the protocol. Subsequent months were spent on official correspondence, data collection, data analysis, report writing and submission of report.

3.5 Sample design

A sampling design is a definite plan for obtaining a sample from a given area. It refers to the technique of the procedure the researchers would adopt in selecting items for the sample.

In this survey the prescription are collected from both outdoor and indoor patient in the hospital. the patients who are visiting general practitioner and specialist doctors also counted. during the period of sampling certain information are extract from the prescriptions to be collected. The information was related to the prescribing of the drugs for specific disorder from which specific disease are recognize.

The criteria to be considered were:

3.6 Inclusion Criteria

In my study both pediatric and geriatric patients are included and the prescription that bears significant impact on

Patient age: 1 day to old aged

Patient sex: Both male and female

Doctors: having specialization on any discipline

Area: Dhaka, comilla, Chittagong, Mymensingh, kushtia, Bhola etc.

3.7 Study Population

From June 2015 through April 2016, total of 1600 prescriptions are collected from government and non-government hospitals specifically from specialist doctors of both male and female patients.

3.8 Data processing and graphical representation

Finally all the collected raw data are processed and represented were analyzed using Windows (Version 16; Chicago, IL) and Office excel (Version 2007).

3.9 Materials

In any kind of thesis work certain kinds of materials are required to express the whole thing. Here certain software has helped me to achieve my goal. Drug data and specialist on specific diseases data were computed using MS-Excel, SPSS and DIMS software. The results were expressed as proportions or as percentages.

3.10 Ethical issues

Prior permission was obtained from the patients or from the carrier of the patients for conducting the stud. This study was done in a manner without conflicting the ethical issues. Ethical consideration was checked by the research supervisor with the research policy of the East West University.

Chapter-IV

Results and Discussion

4 Result

4.1 Table-1: Percentage of prescription containing NSAIDs and multivitamins

Total prescription number: 1600		
Types of drugs	Number of prescription contain target drug	Percentage of total prescription
NSAIDS	541	33.8%
Multivitamins	761	47.5%

On this survey 541 prescription out of 1600 contain NSAIDs .The percentage is 33.8%.Here we also include paracetamol as it is mostly use in case of simple pain and fever.

On this survey 761 prescription out of 1600 contain Multivitamins .The percentage is 47.5%.

4.2 Table-2: percentage of NSAIDS containing prescription in different departments

Specialists / Department	Number of Prescription (NSAIDS)	percentage %
Medicine	285	52.68%
Orthopedics	98	18.11%
Pediatrics	72	13.30%
Gastro liver	25	4.62%
Gynecology	43	7.94%
Dermatology	12	2.21%
ENT	7	1.29%

The above percentage of NSAIDs(including paracetamol) containing prescription in each specialty shows that medicine accommodate the highest area of 52.68% and then the, orthopedics pediatrics, gastroliver, dermatology, gyanecology, ENT as the number of medicine related prescription is high in this study.

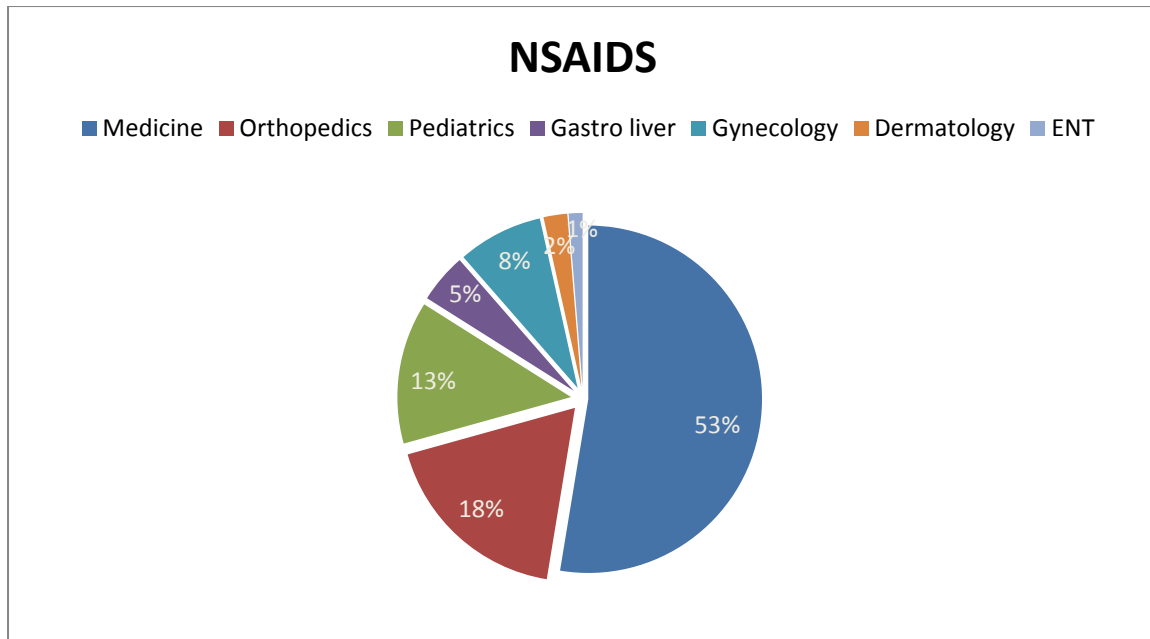
The chart of only NSAIDs containing prescription:

Fig-4.1: percentage of NSAIDs by different departments in Bangladesh

From the above statistical analysis the percentage of NSAIDs in medicine specialist is the highest one (53%) and the orthopedic is the second (18%), third one is pediatric (13%). Others are the less frequent in prescribing antiulcerants. On this study the highest area recognizes medicine specialist.

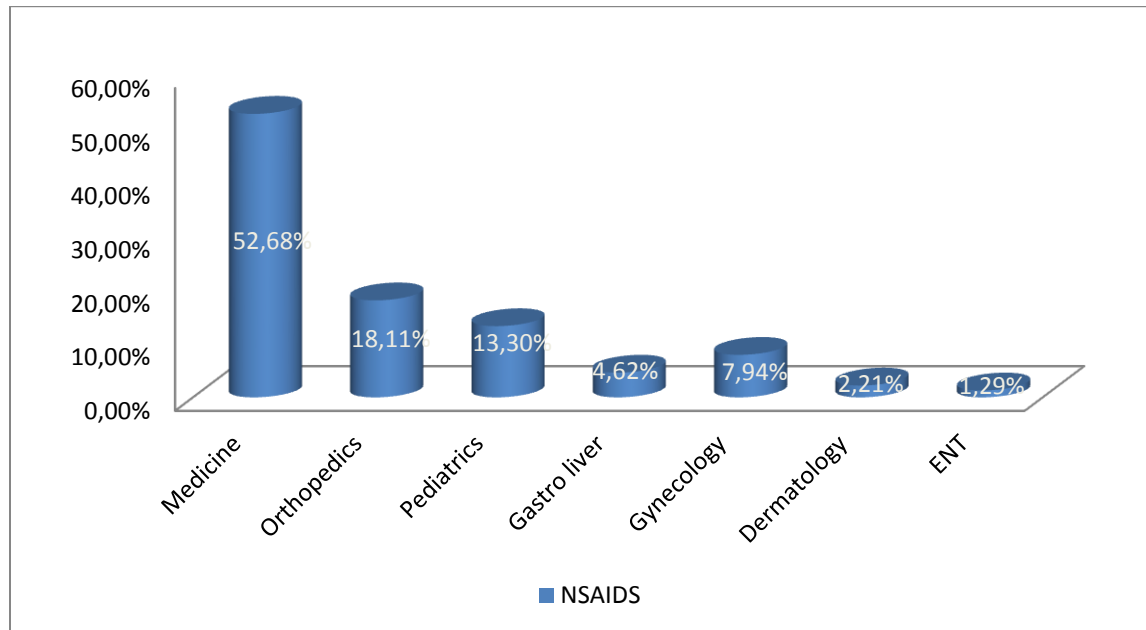


Fig-4.2: column chart of percentage of NSAIDs by different specialist doctors in Bangladesh.

Here in this chart the Y axis indicates the percent of different specialist doctors in Bangladesh that prescribed NSAIDs, and X axis indicates the department.

4.3 Table 3: Percentage of NSAIDs prescribe among a single speciality

Department	Total no of prescription	No of prescription contain NSAIDs	Percentage (%)
Medicine	916	285	31.11%
Pediatrics	157	72	45.02%
Orthopedics	127	98	77.16%
Gastro liver	139	25	17.01%
Gynecology	97	43	44.02%
ENT	70	12	17.14%
Dermatology	94	7	7.29%

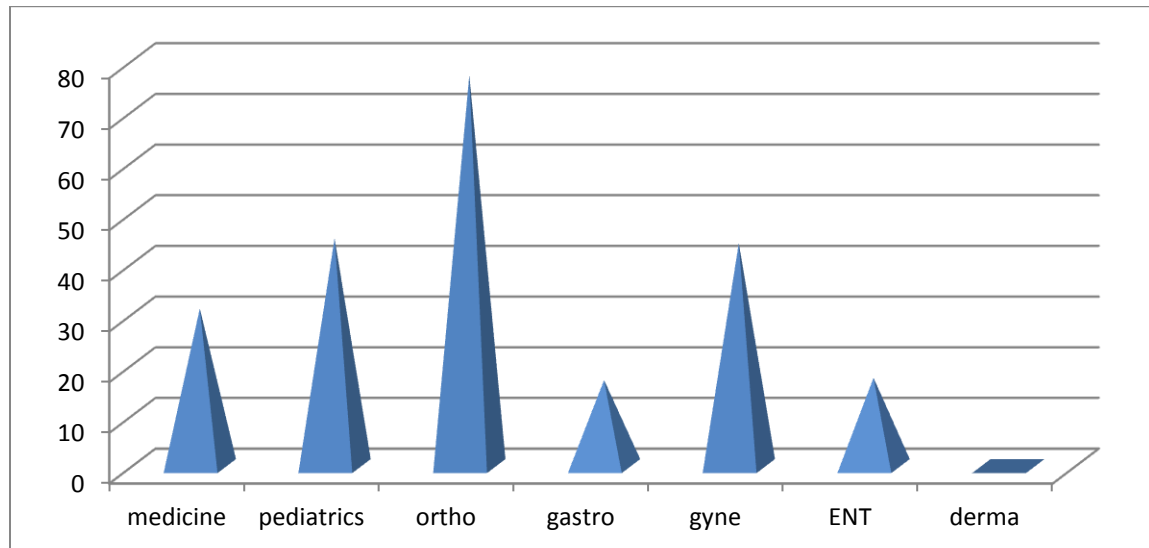


Fig-4.3: column chart of percentage of NSAIDs among single specialist department.

Here in this chart the Y axis indicates the percent of different specialist doctors in Bangladesh that prescribed NSAIDs, and X axis indicates the department.

From above data analysis we found that the highest % of NSAIDs are prescribed in the orthopedic department 77.16%. One of the reasons for this use in orthopedics is more because of its anti-inflammatory property. The medicine 31.11%, pediatrics 45% and gynecology 44% also suggest a significant number of NSAIDs may be due to its safety property is high. The gastro liver suggest NSAIDs very rare because it may induce ulcer.

4.4 Table-3: Percentage of NSAIDs followed EDL(Essential drug list)

NSAIDS in EDL are ibuprofen, morphine, naloxane, paracetamol, pethidine hydrochloride.

Percentage distribution of prescription those followed EDL

Status	Number of prescription (n=541)	Percentage
Followed	292	54.98%
Not followed	249	46.02%

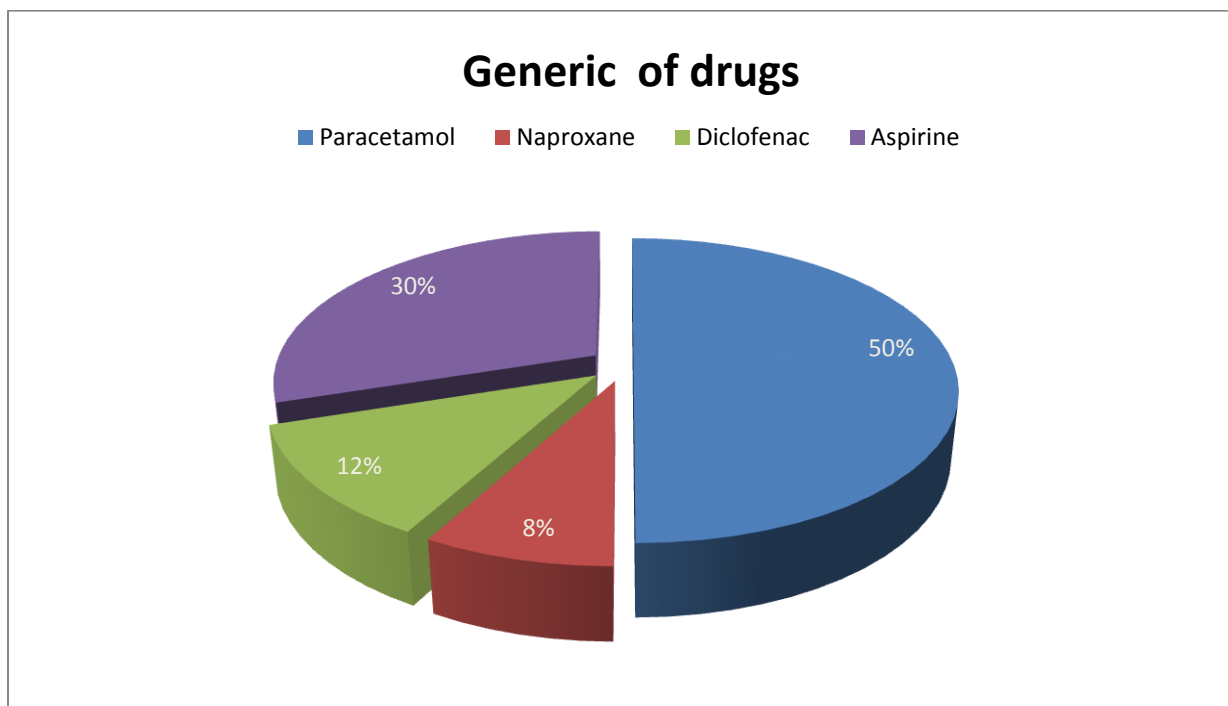
“N= number of prescription containing NSAIDs”.

Among the 541 number of prescription contain NSAIDs only 54.98% specialty followed EDL drug list and 46.02% does not follow EDL. This results shows that a large number of the NSAIDs is prescribed in modern medical prescription and that do not follow the EDL list. This may due to irrational and aggressive promotional activity of the pharmaceutical for their own benefit.

4.5 Table-4: Percentage of different generic prescribed

Generic	Percentage %
Paracetamol	50.03%
Naproxane	8.01%
Diclofenac	12.07%
Aspirin	30.02%

The above percentage of the generic of NSAIDs shows that paracetamol accommodate the highest area of 50.% and then the aspirin contain 30%, diclofenac and naproxen are also found in prescription in little amount.

**Fig-4.4: percentage of generic of NSAIDs by different specialist doctors in Bangladesh**

4.6 Table-5: The shares of different companies NSAIDs from the prescription I have collected

Company name	Percentage %
Square pharmaceutical ltd	21.01%
Beximco pharmaceutical ltd	18.02%
Opsonin pharma	30.01%
Aristropharma ltd	2.05%
Acme laboratories (Aspirin)	25.09%
Renata pharmaceutical ltd	4.03%

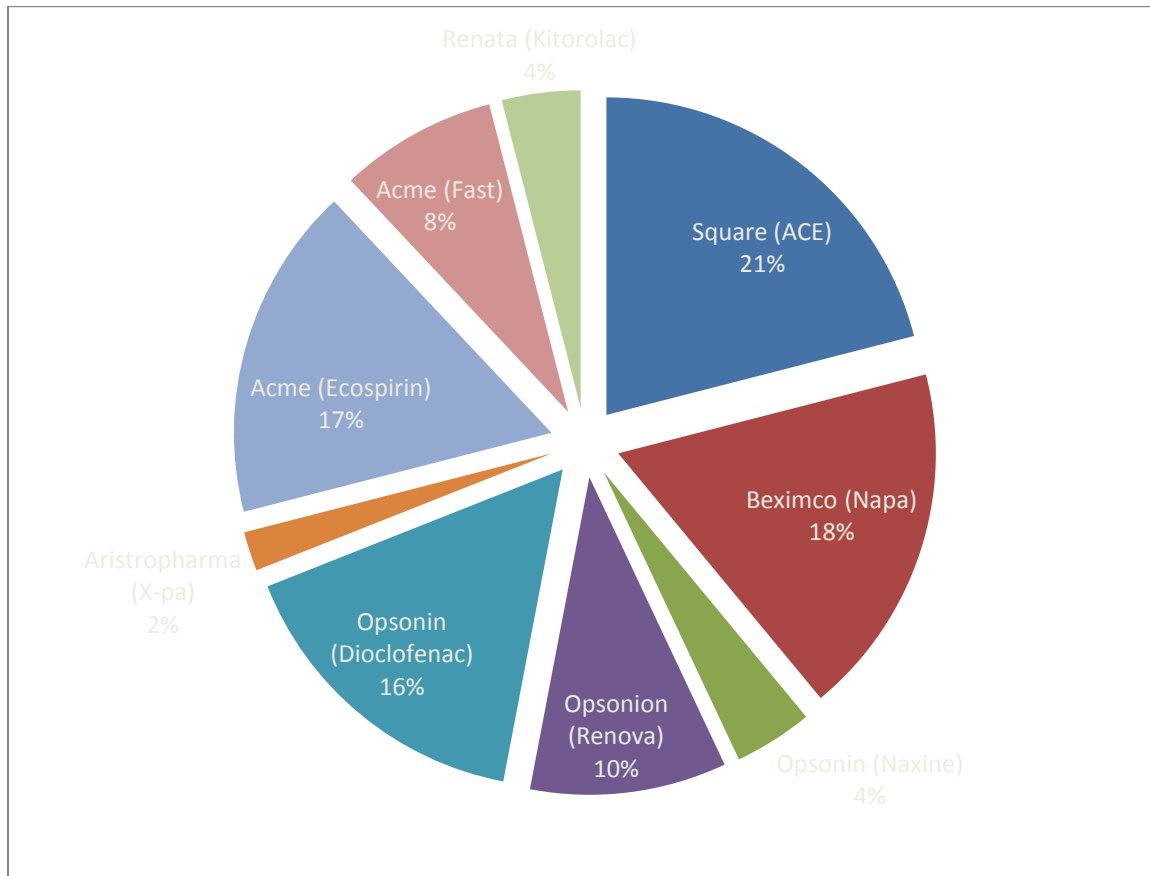


Fig-4.5: The shares of different companies NSAIDs from the prescription I have collected

The above percentage of the brand of NSAIDs shows that ACE 500mg paracetamol tablet is mostly prescribed (21%) and other brands like Napa from Baximco (18%), Ecosprin from Acme (16%) and Diclofenac from Opsonin pharma are highly prescribed. We also observe that Fast from Acme, ketorolac from Renata, Xpa manufactured by Aristopharma are also prescribed in some extend.

4.2 Discussion:

On this survey 541 prescription out of 1600 contain NSAIDs .The percentage is 33.8% the average number of drugs prescribed per patient varied from 0 to 7 with the average of 2.58. This parameter is used to measure the degree of polypharmacy.The most common drugs prescribed in the current study was paracetamol followed by aspirin

Generic prescribing is a potential measure for reducing the cost of drugs. Recently, regulatory authorities of different countries are emphasizing on generic prescribing to cut total healthcare cost. Similar endeavor has also been taken up by local state government. In this backdrop, the percentage of drugs prescribed by generic name in our study was very low.The frequent visit of the medical representatives at health facilities may be the probable cause of the under prescribing of the drugs by generic name.

The percentage of prescription with NSAIDs was found that the highest Percent of NSAIDs were prescribed in the orthopedic department 77.16% .one of the reason of this use in orthopedic more because of its anti-inflammatory property. the medicine 31.11% ,pediatric 45% and gynecology 44% also suggest a significant no of NSAIDs may be due to its safty property is high .The gastro liver suggest NSAIDs very rare because it may induce ulcer.

The percentage of the brand of NSAIDs prescription shows that ACE 500mg pracetamol tablet is mostly prescribed (21%) and other brands like Napa from Baximco (18%),Ecosprin from Acme(16%) and Diclofenac from Opsonin pharma are highly prescribed. We also observe that Fast from Acme,ketorolac from Renata, Xpa manufactured by Aristopharma are also prescribed in some extend,..This clearly indicates the dominating of big company.

The overall percentage of drugs prescribed from an EDL is a measure to examine the degree to which the practices confirm to national drug policy, as indicated by prescribing from national EDL for NSAIDS was 54.%. Ideally, it should be 100% in Bangladesh. The reasons for such wrong practices in our study were inadequate supply of drugs at health centers and unavailability of copy of EDL and their practice.

4.3 Limitation:

Drug prescribing patterns in the present study were not linked with the diagnosis (indication) of the patients because such documents were not kept in the outpatient departments of the hospitals. If it were possible to link them, it would be easy to judge the degree of rationality of the drug prescriptions and their utilization. Association between the age of the patients and type of medications prescribed was also not made due to the same reason. All places in the country cannot be covered. Here the admitted patient prescriptions are not included. If these were possible, it would be easy to judge the degree of rationality in prescribing patterns. However, we believe that this study can be used as a baseline for such comprehensive studies in the future, if patient diagnosis and medication history are documented appropriately.

Chapter-V
Conclusion and Future
Direction

5.1 Conclusion

NSAIDS and multivitamins are commonly prescribed in our country. This research has brought out that Aspirin are most commonly prescribed NSAIDS in our country. We also found the mostly prescribed paracetamol although it is not included in NSAIDs category. This outcome of the study also shows that the significant in adherence with EDL List. So list of Essential drug need to be updated. We also found that motivation and effort is required for the health care professional to prescribe from EDL specially for poor people. Furthermore the capacity and strength of the regulatory affairs need to be improved and revised.

Generally, drug-prescribing practices of hospitals in this study need improvement in light of the WHO prescribing indicators. Particularly, the significant deviation from the acceptable WHO standard in prescribing NSAIDS and multivitamins medications requires special attention. It seems that interventional measures are needed to improve the drug-prescribing patterns in these areas.

However, since the indications and duration of treatments were not included in this study, further study is recommended to better judge the rationality/irrationality of use of much NSAIDs and multivitamin drugs. So in conclusion further more nation wide multicentre study and research with larger sample should be conducted to consolidate the observation.

Chapter-VI

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ANNEXURE

উদ্দেশ্য নিয়ন্ত্রণ ও ব্যায়াম করবেন

• Tab. Diaplus (5).

২+০+২/২ - চন্দ্র.

(১১৩২৩০ ২/২ ঘণ্টা
দুট).

• Tab. Nobelit (৪০০ ৪৫০)

০+০+২/২ - চন্দ্র.

(১১৩২৩০ ৩য়).

• Tab. Cal-D
২+০+২ - ৩ ঘণ্টা.

(১১৩২৩০ ৩য়).

ABF Ecus
HDL, LDL
nine
R/E, Cls

Dr. Shehezen Amin
Medical Officer
Medicine OPD
DDPM

২০

OT given
20.01.16

সব

11 - Ced treatment 10m ②

দুঃ

11 - Naxpro-40-①

প্র

11 - Etforce-30-①

Fresh order on 21.01.16
10.00pm

Diet Normal

Unit - inj-Taxyl - 500mg
1 Amp /m stat & 8

cap. Flucloz-500mg
1+1+1+1

supply - Tab. pantony-200
1+0+1 (A/C)

Tab. Milam 25mg
0+0+1.

supp-voltalin-50mg
Istrek plr stat

BY ORDER

Please transfuse...
initially at...
occur then...
that...
Let call the duty doctor

Name - Raju.

Age - 23 yrs

Reg. No - 349/5

Bag No - 1085

Blood group - A(+ve)

Donor's name - gadol.

Date - 23.1.16

Time - 2.40pm.

Adv:

Blood transfusion - 1 unit

P/A - 23.01.16

Tab. Amoxicillin
1+1+1

Treatment sheet for Specialist Clinic

Date : 19-06-2014
 Name : OLI AHMED Patient ID : 194733
 Age : 21 Year(s)
 Address : SM-17 Gender : Male

Acute pharyngitis

Chief Complaints & Findings	Treatment and Advice
	Rx, (i) Xylomet nasal drop 0.05% ২২ ফোঁটা (২বার ১১ফোঁটা - ৭দিন) (ii) Flunoxone nasal spray ২২ ফোঁটা (২বার ১১ফোঁটা - ৭দিন) (iii) Tab. Martel (10mg) ০ + ০ + ৩ - ২বার X (iv) Tab. Napa (500mg) ৩ + ৩ + ৩ (৩বার ৩০০মি) - ৩বার ৩দিন (v) Tab. Levomax (500mg) ০ + ০ + ৩ - ৭দিন X (vi) Tab. AlbendS ০ + ০ + ৩ (৩বার ৩০০মি) - ৩বার ৩দিন (vii) Tab. Tydosal (500mg) ৩ + ০ + ০ - ৭দিন Dr. Kamran 19-06-14.

কমসার্ধে হাসপাতালে আসবেন তখনই এই ব্যবস্থাপত্র সঙ্গে নিয়ে আসবেন।
 এই টিকেটের মেয়াদ ৭ দিন

Tab Rivostriol (0.05 mg)
 ০ + ০ + ৩ - ৩বার
 Prospan E ID
 ৩ ফোঁটা ৩বার
 Napa ২০০ -
 ৩ + ৩ + ৩ - ৩বার
 ২ (৬৫০ - ২) ৭দিন
 ৩ + ০ + ০ - ৭দিন
 Dr. Kamran
 20.2.14

1. Medication
 2. History
 3. Physical Examination
 4. Laboratory Investigations
 5. Imaging
 6. Special Studies
 7. Response to Treatment
 8. Follow-up
 9. Prognosis
 10. Prevention


F-5.8
 P.P = $\frac{140}{80}$
 Rx
 ① I₂ Menthol/40
 12+0+0 (±0)
 ② T₆ Osaad 150
 1+0+0
 ③ T₆ Ataral 10
 0+0+1
 ④ T₆ pantonax 10
 1+0+1
 ⑤ T₆ Atos 3 senior
 0+1+0


 বাংলাদেশ ফরম নং ৭৬৯ এর পরিধারে
 কুর্মিটোলা জেনারেল হাসপাতাল, কুর্মিটোলা, ঢাকা।
 মূলা-১০/- চিকিৎসা পরামর্শপত্র

১১২
 ৫৫০৫৪! তারিখ ২০/১২

রোগীর নাম : আব্বাস
 রোগীর ঠিকানা : ২৮৮
 বয়স : ২৯
 রোগী : ১-২০৪
 রোগের সংক্ষিপ্ত বিবরণ : AD

For Deslor (50)
1.0 to 1.0 - 1.0 hr
For Momet (10)
0.1 to 0.1 - 1.0 hr
 ১০.২.১৬
 চিকিৎসকের স্বাক্ষর


 বাংলাদেশ ফরম নং ৭৬৯ এর পরিধারে
 কুর্মিটোলা জেনারেল হাসপাতাল, কুর্মিটোলা,
 মূলা-১০/- চিকিৎসা পরামর্শপত্র

৫৫২৩১! তারিখ ১০/১২

রোগীর নাম : আব্বাস
 রোগীর ঠিকানা : ২৮৮
 বয়স : ২৯
 রোগী : ১-২৬৮

রোগের সংক্ষিপ্ত বিবরণ :
For Deslor
0.1 to 1.0
Antepral Mid
8.2 to 1.0 hr

২৫০ শয্যা বিশিষ্ট হাসপাতাল, মৌলভীবাজার।
250 Bedded Hospital, Moulvibazar.

ছাড়পত্র

DISCHARGE CARD

রোগীর নাম: বিদ্যা রেজিঃ নং: ৬৩০০
 পিতার/স্বামীর নাম: বল্লভ তারিখ: ০২/০২/১৬
 বয়স: ৩০

ঠিকানা: গ্রাম: শুভাবি পো:
পানার: বাজার হাজিরা: কী. ম. ক.

উদ্ভাষিত রোগী/রোগীনি অথবা হাসপাতালে প্রসূতি: বিভাগে: নার্সিং ওয়ার্ডের: ৩/৬
 শাখা/কোষ: তারিখ: ০২/০২/১৬ হইতে ০২/২/১৬ তারিখ পর্যন্ত ভর্তি ছিলেন।
 এবং তিনি 2nd trimester RTP LP রোগে ভুগিতেছিলেন।

চিকিৎসার পরামর্শ:

NVD 31.01.16 Bby note
 wt. 10:30 pm sex Female
 wt. 3.4kg
 ALS ১/১০

 Tub. Furcocef (200mg) ১দিন
 ১+০+১
 Tub. metwyl (400mg) ১দিন
 ১+০+১
 Tub. Domin (60mg) ১২mm
 ১+০+১
 Tub. Rolat (60mg) ১দিন
 ১+০+১
 Tub. Finix (60mg) ১২mm
 ১+০+১
 Tub. Calcin-0 6mm
 ০+০+০
 Cap. Ferix 6mm
 ০+০+০
 Tub. ceevit ১দিন
 ১+০+১

চিকিৎসকের পরামর্শ অনুযায়ী চন্দ্র, সু-বাহ্য নিশ্চিত করুন।

250 Bedded Hospital, Moulvibazar.

ছাড়পত্র

DISCHARGE CARD

রোগীর নাম: রেজিঃ নং: ৫০৫০
 পিতার/স্বামীর নাম: তারিখ: ২৬/০২/১৬
 বয়স: ২৪

গ্রাম: পো:
 জেলা:

উদ্ভাষিত রোগী/রোগীনি অথবা হাসপাতালে প্রসূতি: বিভাগে: ওয়ার্ডের:
 শাখা/কোষ: তারিখ: হইতে তারিখ পর্যন্ত ভর্তি ছিলেন।

তিনি রোগে ভুগিতেছিলেন।
 চিকিৎসার পরামর্শ: Bdy note
 NVD 31.1.16 sex - M
 wt - 2.5 kg
 ALS - ১/১০

 Tub. Furcocef 200 ১দিন
 ১+০+১
 Tub. Maxho 20 ১দিন
 ১+০+১
 Tub. Domin 10 ১দিন
 ১+০+১
 Tub. Calcin-0 ১দিন
 ১+০+০
 Cap. Ferix ১দিন
 ০+০+০
 Cap. Anadol 10 ১দিন
 ১+০+১

