KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, KUMASI
COLLEGE OF HEALTH SCIENCES
FACULTY OF PHARMACY AND PHARMACEUTICAL SCIENCES

ANALGESIC USE AT THE POLYCLINIC OPD OF KOMFO ANOKYE TEACHING HOSPITAL

by

Sarah Arthur Owusu-Ansah
B Pharm (Hons)

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A Thesis submitted to the Department of Clinical and Social Pharmacy,
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DECLARATION

I hereby declare that this submission is my own work towards the MSc and that, to the best of my knowledge, it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the University, except where due acknowledgement has been made in the text.

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Student Name & ID	Signature	Date

Certified by:

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Supervisor(s) Name	Signature	Date

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Head of Dept. Name	Signature	Date

DEDICATION

I dedicate this work to my family, especially the children, David and Debbie, who have been patient with me during my absences from home.

ABSTRACT

Objective: This study was conducted to determine which analgesics were commonly prescribed at a busy polyclinic as well as to document the conditions for which they were prescribed, their availability at the polyclinic pharmacy and also to pick out any cautionary cases.

Method: The study was a descriptive prospective cross-sectional study over a period of 4 weeks from mid December 2006 to mid January 2007. A purposeful sampling method was employed, ie. twenty consecutive prescriptions containing analgesics for each day were included in the data collection. Data was extracted from the prescription forms and filled on the data collection form. Numbers and percentages of the data were calculated using the electronic data processing software SPSS (version 12).

Setting: The general out-patient consulting rooms and pharmacy of the polyclinic of Komfo Anokye Teaching Hospital, Kumasi.

Key Findings: A total number of three hundred and forty analgesic prescriptions were collected during the period of study. The most commonly prescribed analgesic was paracetamol (52.8%). NSAIDs followed at 40.1%. Diclofenac was the most common NSAID prescribed at 68.9% of all NSAIDs prescribed. The commonest documented indication for NSAIDs was malaria (34.5%) followed by hypertension at 25%. The rationale for the use of NSAIDs in hypertension was however not clear.

Malaria was the most common indication for analgesic prescribing in all age groups at 67.5%. The majority (34.1%) of all the prescriptions were for age groups of 15-45 years but the age group 45-65 years followed at 23.3%. In addition 62.7% of all paediatric prescriptions under five years were for males. Malaria was the commonest indication in

children under five at 83.1% and the mean duration of therapy was found to be approximately 5 days.

Generic prescribing was generally good at 79.1% whiles 95.7% of all drugs were available at the pharmacy. Also 94.3% of all drugs prescribed were in line with the hospitals Drugs and Therapeutic Committee's recommended list.

Conclusions: A high percentage of NSAID prescriptions were going to hypertensive patients over 45 years. The mean duration of days for paracetamol use in paediatric patients may need to be examined. Generic prescribing, drug availability and adherence to Drug and Therapeutic Committee drug list were however very high and thus commendable.

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ACKNOWLEDGEMENT

This work would not have been completed without the support of my supervisors, Professor Mahama Duwiejua and other lecturers of the Department of Clinical and Social Pharmacy, staff of the pharmacy at the Komfo Anokye Polyclinic – both sections, valuable and critical contributions especially from Mr. Kwasi Appiah, Clinical Pharmacist, Komfo Anokye as well as the green light given by Mrs. Anima-Appiah, Head of the Pharmacy Department and the Ethics Committee of the Hospital.

CHAPTER ONE - INTRODUCTION

1.1 Introduction A wide range of disease conditions involve an element of pain as a symptom. As a result, analgesic prescribing as an adjunct to therapy is widely practiced. The alleviation of pain thus is an important part of the perception of cure and the overall well-being of the patient.

The most commonly prescribed analgesics include the non anti-inflammatory analgesics like paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) like diclofenac and opioid and opioid-like analgesics such as codeine and tramadol as well as various compounds preparations containing the afore-mentioned products in different combinations.

In a setting such as the polyclinic, prescribers who attend to patients include mostly general medical practitioners and house-officers. Complicated cases and other cases which will require further monitoring are referred for specialist attention either at the specialist outpatient departments (OPDs) or admitted to the appropriate wards. In almost all cases, pain alleviation becomes an important part of the therapy and compliance of the patient to other prescribed medication.

The ultimate goal of drug utilization research is to assess whether drug therapy is rational or not [1], thus drug utilization studies are important tools to evaluate whether drugs are used properly in terms of efficacy, safety, convenience and economic aspects at all levels in the chain of drug use. Regardless of considerable improvements in the availability and control of drugs in hospitals, rational drug use is still a worldwide problem [2].

Information about drug utilization in Africa in general, and in Ghana in particular is scanty. That concerning analgesic use in particular remains little or unknown.

In Northwest Ethiopia, a study by Desta, Gebre et al (2002) found that analgesic prescribing (11-49%) followed antibacterials (40-51%) as the most commonly prescribed agents. [3] A retrospective review of almost fifty thousand prescriptions in a primary health care setting in South Africa showed 12.2% of agents prescribed were analgesics and most of these were for non-opioid analgesics. [4].

Akande and Ologe in Ilorin, Nigeria showed in a descriptive cross-sectional survey that analgesics accounted for 19.7% of all drugs prescribed.[5]. Similar studies on analgesic use in Ghana are however not available.

1.2 Study goals and objectives:

The goal of this study is to investigate the analgesic prescribing pattern at the polyclinic OPD of KATH, focusing on the consulting rooms which attend to general medical cases. In addition the conditions for which they are prescribed will be documented in addition to evaluating whether prescribers adhere to the recommendations of the Drugs and Therapeutic Committee (DTC). The general / medical consulting rooms will be focused upon as they provide a concentrated area for various conditions, providing a broad over view of the general prescribing trend. It will also offer an opportunity to evaluate the range of analgesics offered at the pharmacy to establish whether there is a correlation between prescribing pattern and stocking.

1.3 Importance of study: This study is intended to identify the most common analgesics prescribed at a general polyclinic and thus inform the hospital administration on any need to come out with guidelines to prescribing analgesics. It is also intended to aid the pharmacy in determining which particular products to stock and thus assist in budgeting of limited funds.

Any cautionary situation will also be assessed and thus aids in alerting general prescribers on such trends and hence improve prescribing habits

1.4 Objectives of the study:

1. To determine the most commonly prescribed analgesics
2. To document the conditions for which they are prescribed
3. To investigate the availability of such analgesics at the pharmacy
4. To document any cases where caution should be observed
5. To check general adherence to analgesics on the Hospital's drug list.

CHAPTER TWO – PAIN AND PAIN MANAGEMENT

2.1 PAIN

Definition and Meaning of pain: According to the International Association for the Study of Pain, pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." [6] Furthermore "Pain is always subjective. Each individual learns the application of the word through experiences related to injury in early life." [6]

Pain has broadly been classified into acute pain and chronic pain depending on the duration of the sensation of discomfort. Acute pain is pain that lasts or is anticipated to last a short time, typically less than a month and is associated with anxiety and hyperactivity of the sympathetic nervous system (e.g. tachycardia, increased respiratory rate and blood pressure, diaphoresis and dilated pupils) [7]. Chronic pain is pain persisting more than one month beyond the resolution of an acute tissue injury, i.e. pain persisting or recurring for more than three months, or pain that is expected to continue or progress [7]

Most tissues and organs are served by special sensory receptors (nociceptors) connected to primary afferent nerve fibres of different diameters. Small myelinated Aδ fibres and unmyelinated C fibres are believed to be responsible for the transmission of painful stimuli. Various neurotransmitters may also be involved in pain modulation, including γ-aminobutyric acid (GABA), noradrenaline and 5-hydroxytryptamine (5-HT). [8]. Acute pain is often self limiting and can be managed by analgesic drugs. Chronic

pain treatment can be more complex and involve pain clinics and a multi disciplinary approach which manages medical and behavioral aspects. [8]

The Pain Pathway:

The production of a pain reaction involves four major steps: transduction, transmission, perception and modulation (9). A stimulus is converted to an action potential (transduction) which is then transmitted along the length of the neurons to the dorsal horn of the spinal cord (Fig 2.1). The transmission of impulses from the site of injury to the central nervous system is called nociception. Chemical interactions may enhance or inhibit the transmission of nociceptive information at all points along this transmission (10).

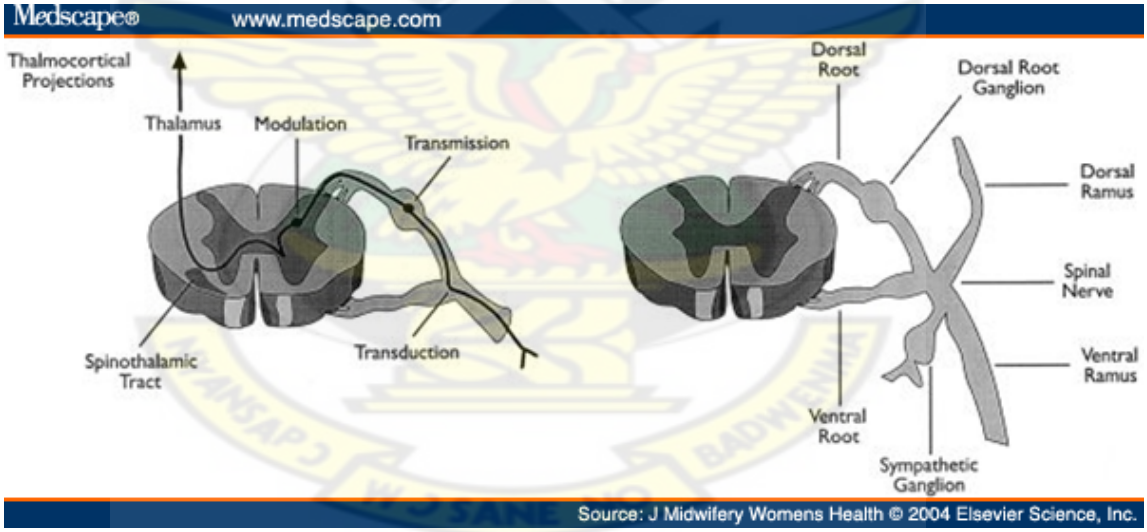

Figure 2.1 Pain Modulation Pathways

In the dorsal horn, processing of the signal results in the release of various neurotransmitters from the afferent fiber into the synaptic cleft. These neurotransmitters then facilitate or inhibit further transmission of impulses. The ultimate perception of

pain occurs in the cerebral cortex. Pain perception itself is a totality of the autonomic response to stimulus, the somatosensory localization (ie the area of consciousness) and the characterization of pain as well as the emotional and behavioural components contributed by the limbic system. Pain modulation is the inhibition or facilitation of pain via the activation of modulatory fibers or pathways (9).

Psychological aspects of Pain: It is said that reporting pain is more socially acceptable than reporting anxiety or depression. [7]. Pain experienced means different things to different people. Beecher in his work with injured soldiers during World War II and subsequently among civilians found that soldiers were less likely to complain of enough pain requiring use of morphine as against civilians with comparable injuries. He concluded that the meaning attached to the injuries in the two groups explained the different levels of pain. To the soldier, the wound meant surviving the battlefield and returning home whiles the injured civilian often faced major surgery and loss of income, diminished activities and other negative consequences [11]. It becomes necessary therefore for a prescriber treating pain to look beyond organic causes where necessary.

Pain as a symptom: The top ten disease states in Ghana include malaria, respiratory tract infections, as well as skin diseases and accidents [12]. A look at the catalogued symptoms of these conditions shows that pain in one form or another stands out as a symptom. [13]

The Standard Treatment Guidelines for 2004 also points out that the underlying cause for headaches, a common symptom, should be treated before offering analgesia. [14]. In

Ghana the costs of pain therapy is not available but in the United States for example, it has been estimated that $100 billion is spent annually on pain therapy [9] Managing pain is therefore an essential part of clinical practice, contributing to the overall cure or feeling of wellbeing of the patient.

2.2 PAIN MANAGEMENT

Treating pain – Analgesics: In the out-patient setting, a patient reporting with a condition which has pain as a symptom is often offered analgesia in the form of medication to help relieve symptoms. Classification of analgesics is generally into non-opioid analgesics and opioid analgesics. [7] Opioid is a generic term for natural or synthetic substances that bind to specific opioid receptors in the central nervous system, producing an agonist action [7]. The other commonly prescribed analgesics are subsequently termed **non-opioid** and include non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol.

2.2.1 Opioid analgesics:

Opioid analgesics act on both central and peripheral nervous systems. In the central nervous system, they have effects on many areas including the spinal cord, whereas in the peripheral nervous system they act on both the myenteric plexus and sub mucous plexus in the wall of the gut as well as in the joints to reduce inflammation (15). Three major types of opioid receptors – μ, δ and κ (mu, delta and kappa) were defined pharmacologically several years ago. All three of these receptors produce analgesia

when an opioid binds to them; however physical dependence depends on activation of the κ receptors.

Naturally occurring opioids include β-endorphin, which interacts preferentially with μ receptors, the encephalins which interacts with δ receptors and dynorphin with κ receptors. Morphine has considerably higher affinity for μ receptors than for other opioid receptors (15) (explaining its potential for abuse and dependence).

Opioid receptors are present in many regions of the nervous system that are involved in pain transmission and control. As a result, under pathological conditions, the endogenous opioid system is activated to help deaden the sense of pain.

The opioid drugs produce analgesia by actions at several levels of the nervous system, in particular, inhibition of neurotransmitter release from the primary afferent terminals in the spinal cord and activation of descending inhibitory controls in the midbrain [15].

Use and side effects: Opioid analgesics are usually used to relieve moderate to severe pain particularly of visceral origin. Repeated administration may cause dependence and tolerance. Opioid analgesics share many side effects though qualitative and quantitative differences exist. The most common include nausea, vomiting, constipation and drowsiness. Larger doses produce respiratory depression and hypotension [16]. Opioids used as analgesics on the approved drug list of KATH include morphine, dihydrocodeine, pethidine and tramadol.

Uses : Morphine is the opioid of choice for severe pain especially in palliative care. **Dihydrocodeine** is effective for the relief of mild to moderate pain comparable to codeine. It is given usually 30mg every four hours.

Pethidine produces prompt but short acting analgesia; it is less constipating than morphine but even in high doses is a less potent analgesic. It is not suitable for severe continuing pain [16].

Tramadol produces analgesia by two mechanisms – an opioid effect and an enhancement of serotogenic and adrenergic pathways. It has fewer of the typical opiod side effects (less respiratory depression, less constipation and less addiction potential) however psychiatric reactions have been reported.

Doses of opioids may need to be adjusted individually according to the degree of analgesia and side-effects; patient's response to opioids varies widely

At the polyclinic OPD, tramadol was the only prescribed opioid –like agent recorded as being given on an outpatient basis.

2.2.2 Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

Another group of analgesics in common use are the NSAIDS. The term NSAID is an abbreviation for "non-steroidal anti-inflammatory drugs". This term is used to differentiate them from steroids, which are also anti inflammatory drugs, but are not analgesics or antipyretics. NSAIDS are very important in the management of pain in adults and adolescents because of their dual anti inflammatory and analgesic actions.

NSAIDS as Anti inflammatory agents: Inflammation can be considered as an event of immune response to tissue damage, which is accompanied by the release of several biochemical mediators including histamine, bradykinin, platelet activating factor and a group of lipid material known as leukotrienes and prostaglandins (17). It is these

mediators which are responsible for the symptoms that accompany the inflammation process. Histamine, bradykinin and leukotrienes cause swelling and redness whiles prostaglandins increase tissue sensitivity to pain and elevation of body temperature (Fig 2.2)(17)

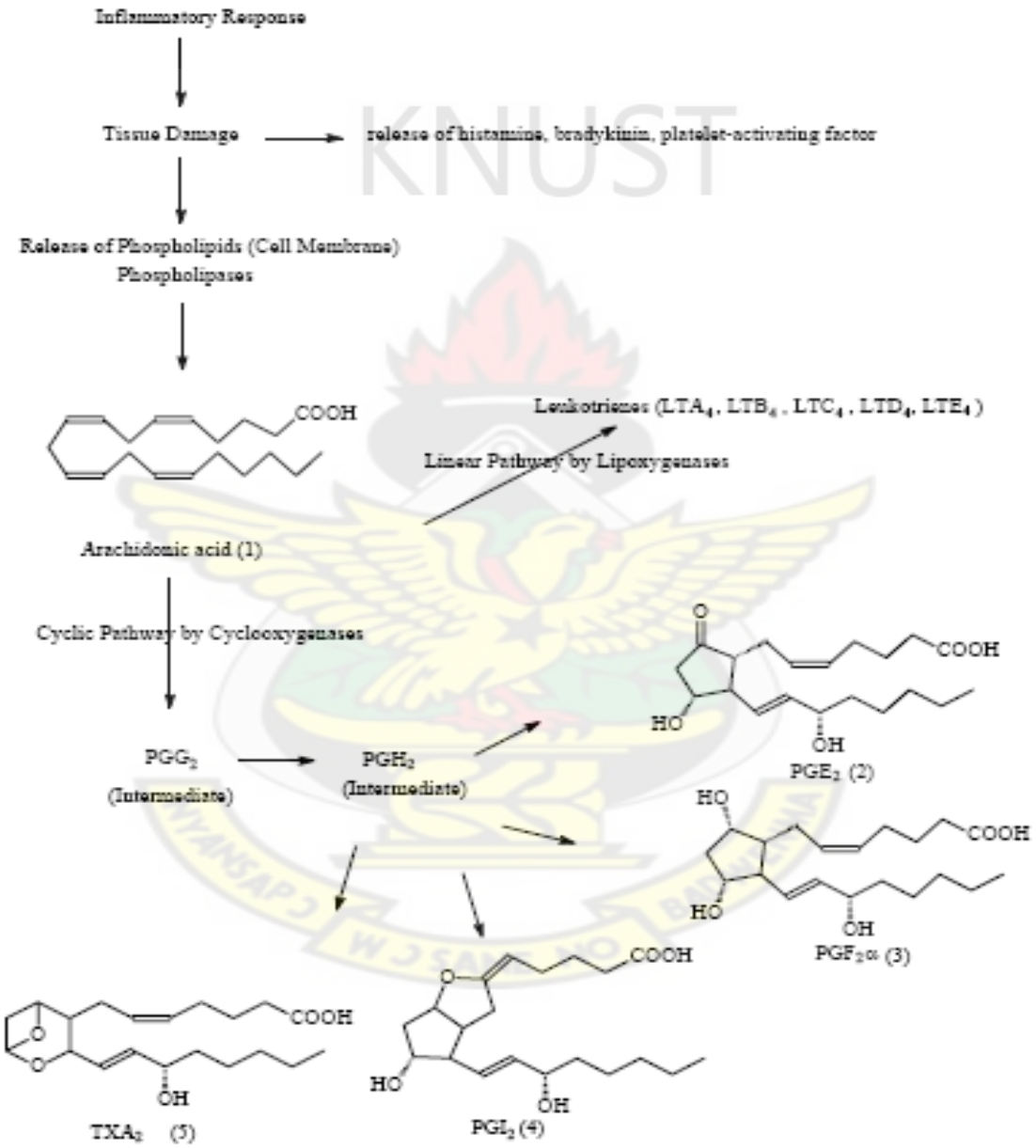

Figure 2.2: **Inflammation cascade and Formation of prostaglandins and leukotrienes from arachidonic acid (from American Journal of Pharmaceutical Education 2003; 67(2) Article 63)**

NSAIDS act by competitively antagonising arachidonic acid thereby reducing prostaglandin synthesis through the inhibition of cyclo-oxygenase enzymes. All NSAIDS are effective in this effect by possessing high lipophilic and acidic properties to mimic the natural substrate chemistry. Examples of these are shown in Fig 2.3 - ibuprofen (structure 6), flubiprofen (structure7), ketoprofen (structure8), naproxen (structure9), indomethacin (structure10), diclofenac (structure11), and piroxicam (structure12).

NSAIDs and Ulcers: NSAIDS in general exhibit a similar pattern of adverse effects on the gastrointestinal tract including nausea, vomiting and diarrhoea. The most serious and detrimental adverse effect attributed to prolonged use is however the development of gastric ulceration (17) This property is due to their structure as organic acids and also due to their inhibitory effect on prostaglandin synthesis. Naturally, prostaglandins stimulate the production of mucin, a mucosal secretion which acts as an endogenous cytoprotective substance against the digestive effects of trypsin and hydrochloric acid. Reduced mucin secretion leads to an increased risk of ulceration. The discovery that COX enzyme has two subtypes COX-1 and COX-2, with COX-1 existing throughout the biological system including the stomach, whiles COX-2 is much less abundant in the stomach, has led to the development of selective COX 2 inhibitors which attempt to minimize the ulcerogenic potential of NSAIDS. Two major drugs produced by this approach are celecoxib and rofecoxib (Fig 2.3 - 19 & 20)

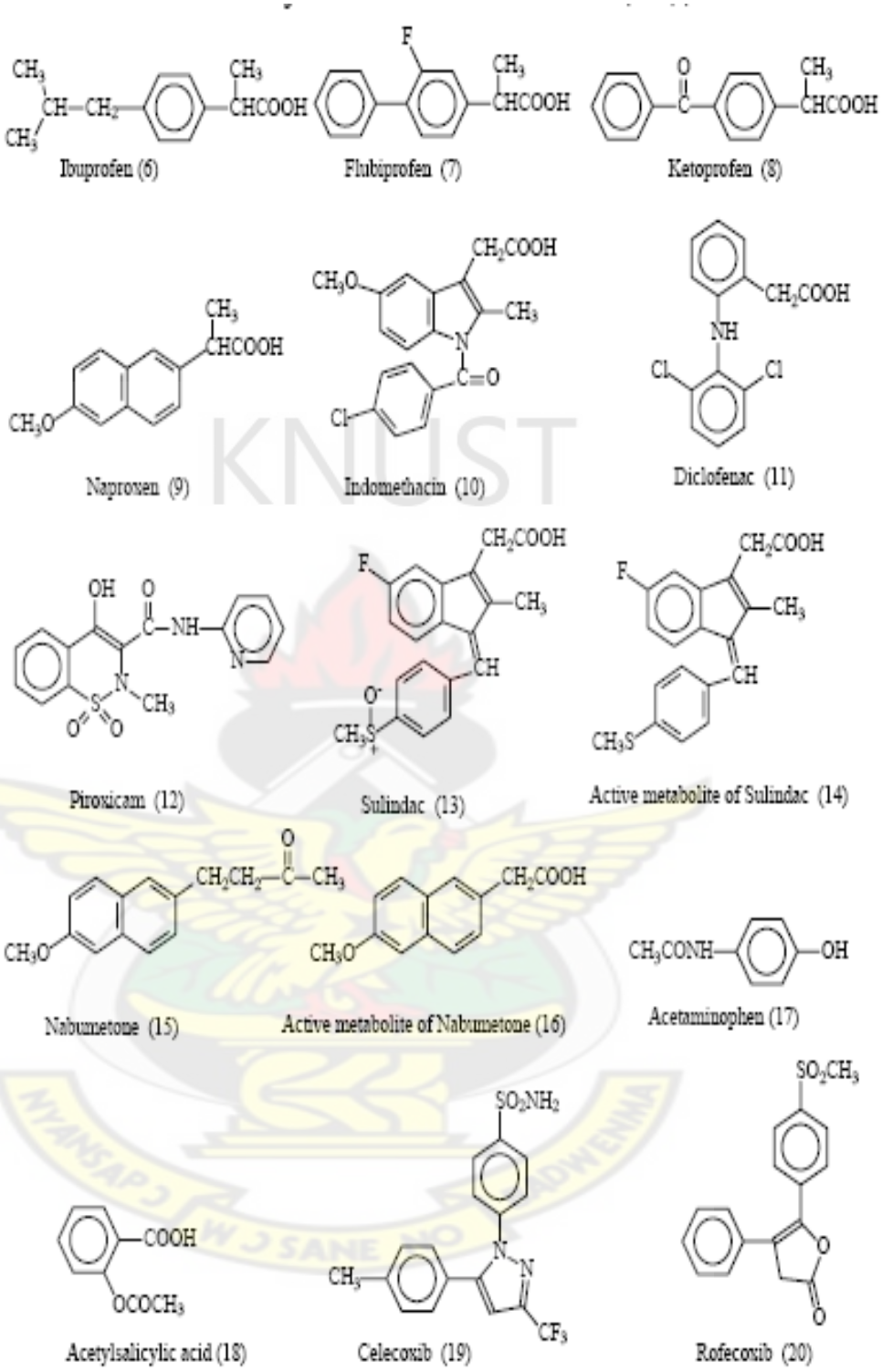

Figure 2.3: Structures of some typical NSAIDs and COX-2 inhibitors (from American Journal of Pharmaceutical Education 2003; 67(2) Article 63)

OTHER EFFECTS OF NSAIDS

Blood clotting: Clinically, NSAIDS primarily increase bleeding through the inhibition of thromboxane. If a peptic ulcer is also present, this constitutes a serious problem, which is not alleviated by the use of COX-2 selective drugs. However this inhibitory effect on clotting is clinically useful in the application of aspirin as a prophylactic agent against thrombolytic stroke. (18)

Renal Effects: NSAIDS have renal altering actions through their effects on renal prostaglandins. COX-1 prostaglandins are responsible for maintaining the integrity of the gastrointestinal mucosa, platelet adhesion and acid secretion whiles COX-2 related prostaglandins largely mediate pain and inflammation. In addition COX-1 also functions in the control of renal haemodynamics and glomerular filtration rate (GFR) whiles COX-2 functions affect salt and water secretion. These renal effects are mediated through prostaglandins E2 and I2.

In a person with normal renal haemodynamics, prostaglandins do not play a dominant physiologic role in maintaining renal blood flow. In compromised however, the kidney synthesises vasodilating prostaglandins to offset the effects of vasoconstricting autacoids and maintain renal perfusion. When PGI2 is blocked, hyperkalaemia and acute renal failure can result. Blockade of PGE2 may also lead to peripheral oedema, increased blood pressure, weight gain and (rarely) congestive heart failure (19).

In view of the above, patient groups who are at risk for adverse renal effects can be identified. At high risk are those with extreme liver dysfunction, nephrotic patients with high level proteinuria or those with very low renal function and these effects are also applicable to COX-2 selective inhibitors. In addition, NSAIDS can significantly reduce

renal blood flow in a person with decreased circulating volume and hence precipitate acute renal failure. Those at risk include those with age related declines in GFR, those with hypovolumea, and those with congestive cardiac failure, cirrhosis or nephrosis. In addition, drug therapies that cause reversible renal insufficiency may worsen with NSAIDS [17]. Examples include ACE inhibitors and angiotensin II receptor blockers.

Hypertension: NSAIDS, especially non-selective ones can induce dose related fluid retention and raise blood pressure in some patients. An increase of 5mmHg in systolic and diastolic blood pressures has been shown to increase the risk for stroke and heart failure [19].

NSAIDS used at the polyclinic OPD: NSAIDs approved for prescription at the hospital including the polyclinic included ibuprofen, diclofenac, aspirin, indomethacin, piroxicam and naproxen in various formulations. These drugs are also contained in various compound preparations and are found in the Drug and Therapeutic Committee approved drug list.

2.2.3 Paracetamol:

Paracetamol is a p-aminophenol derivative that exhibits analgesic and antipyretic activity. It does not possess anti-inflammatory activity. Paracetamol is thought to produce analgesia through a central inhibition of prostaglandin synthesis. [20] Paracetamol (INN) or acetaminophen (USAN) is a common analgesic and antipyretic drug that is used for the relief of fever, headaches, and other minor aches and pains. Paracetamol is also useful in managing more severe pain, allowing lower dosages of

additional NSAID or opioid analgesics to be used, and thus minimizing overall side-effects. The words acetaminophen and paracetamol both come from the chemical names for the compound: N-acetyl-para-aminophenol and para-acetyl-amino-phenol [21].

Mechanism of action: The exact mechanism for reducing fever and pain by paracetamol remains a source of debate. It reduces the production of prostaglandins like aspirin but unlike aspirin it has little anti-inflammatory action and does not inhibit the production of thromboxanes. It has however been shown to act via at least two pathways [21] as outlined below.

The COX family of enzymes catalyses the metabolism of arachidonic acid to prostaglandin H_2, which is in turn converted to other pro-inflammatory compounds. NSAIDS act by blocking this step. However the COX enzyme is also highly active only when appropriately oxidized and paracetamol has been shown to reduce the oxidized form of the COX enzymes and thus prevent the formation of pro-inflammatory compounds [22].

Also a metabolite of paracetamol, AM404, has been shown to inhibit the uptake of the endogenous cannabinoid anandamide by neurons [23] as well as inhibiting sodium channels in a manner similar to lidocaine and procaine (anaesthetics). Thus by this dual action paracetamol reduces pain. Finally, one theory also is that it also selectively inhibits the COX-3 isoform which has no inflammatory action [24].

Adverse effects: Possible adverse effects of paracetamol include nephrotoxicity, hypersensitivity reactions, neutropenia and thrombocytopenia. Significant hepatotoxicity in over dosage or long term use of doses above the therapeutic dose can occur [25].

2.2.4 Compound Analgesic products:

Several analgesic preparations on the market are a combination of two or more analgesics as well as other adjuvants which have been claimed to enhance the analgesic properties of the other components.

Such combinations include paracetamol with ibuprofen, paracetamol with aspirin, aspirin with caffeine, aspirin with paracetamol and caffeine as well as paracetamol with codeine and paracetamol with some B vitamins.

Paracetamol with opioids: Paracetamol with codeine (co-codamol) or dextropropoxyphene (co-proxamol) are preparations of paracetamol with an opiod which reduce the scope for effective titration of the individual components in the management of pain. In particular, over dosage with co-proxamol is complicated by respiratory depression and acute heart failure due to the dextropropoxyphene and by hepatotoxicity due to paracetamol [26].

Caffeine: Caffeine is a weak stimulant often included in small doses in analgesic preparations. The claim is that the addition of caffeine may enhance the analgesic effect of the other components. In excessive dosage or on withdrawal, caffeine may itself

induce headache, as well as having the undesirable effects of alertness and being mildly habit forming [26].

B vitamins in analgesia: B vitamins can be effective in alleviating neuropathic pain caused by injury to the nervous system. B vitamins, such as thiamine (B1), pyridoxine (B6), and cynacobalamin (B12) have been proven to be clinically effective in treating various painful conditions such as lumbago, sciatica, trigeminal neuralgia among others (27). Nociceptive pain comes from sprains, bone fractures, burns, bruises inflammation (from an infection or arthritic disorder), obstructions and myofascial pain. The pain originates from nociceptors and signal tissue irritation, impending injury or actual injury. Research studies found that noxious heat-evoked nociceptive responses of spinal dorsal horn neurons were suppressed by compound of B1, B6 and B12. These studies indicate that B-vitamins possess the capability to block physical stress in some painful conditions. Research has also shown that B1, B6, B12 and their combinations inhibited chemical and heat induced pain. Various commercial preparations exploit this anti-nociceptive activity by combining these vitamins with paracetamol especially, or metamizol (27).

2.2.5 THE WHO PAIN RELIEF LADDER

To rationalize the use of analgesics in cancer pain, the World Health Organisation came out with the "Analgesic Ladder" aimed at guiding the step-wise use of progressively

potent analgesics. This has however been applied to all pain management situations as outlined below (28):

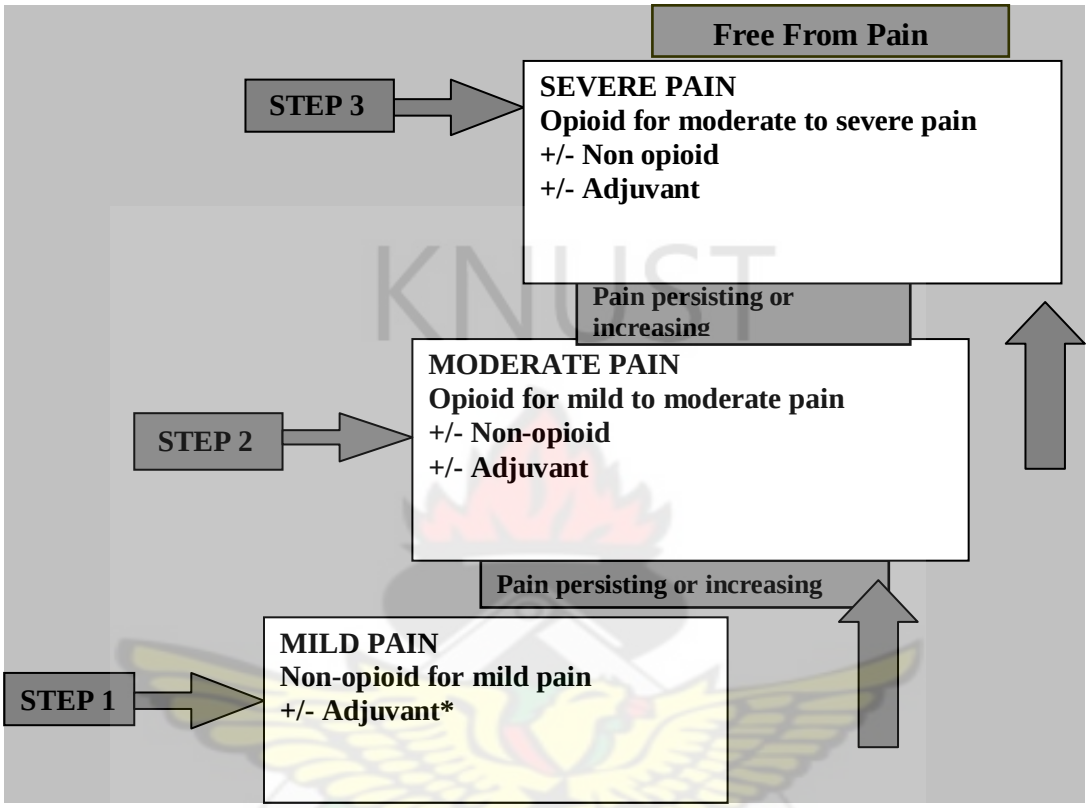

Figure 2.4 WHO Pain relief ladder

If pain occurs, there should be prompt oral administration of drugs in the following order:

- Non-opiod (paracetamol and aspirin), then, as necessary, mild opioids (codeine) then strong opioids such as morphine until the patient is free from pain.

To maintain freedom from pain, drugs should be given "by the clock" rather than on demand.

2.2.6 Acute pain Management

Acute pain occurs as the result of injury to the body tissues. It is the kind of pain that follows trauma, surgery, or self limited diseases. In most cases, acute pain persists only for a limited duration of time and lessens in severity as the healing processes take place. Acute pain is understood and treatment is short-term and curative [29]. It is the focus of this study as a common symptom in an outpatients department.

Pain has also been divided into somatic and visceral pain. Somatic pain refers to pain from soft tissues, bone and joints that contain nociceptors. Visceral pain refers to pain from viscera that do not contain nociceptors and is also termed referred pain. It can act as if it is coming from other structures or as a well-localized phenomenon [29].

Treatment of somatic pain includes the use of paracetamol, cold packs, corticosteroids, localized anaesthetics (topical or infiltrate), NSAIDS, opioids and tactile stimulation. Visceral pain treatments include corticosteroids, intraspinal local anaesthetic agents, NSAIDS and opioids [10]

Another type of pain, neuropathic pain, results from damage to the peripheral or central nervous system from trauma or from disease. It is mediated by a number of different neurotransmitters and is described differently from nociceptive pain. Neuropathic pain is often described as burning, tingling, shooting or lightning-like. This sort of pain is often not very sensitive to opioids at all. Anticonvulsants and tricyclic antidepressants are the mainstay of therapy. [10] These drugs were however not included in this study.

2.2.7 Non-pharmacologic management of pain

Besides medication, there also non-pharmacologic options to control pain, which are used to complement pharmacologic options. Many of these methods do not require a prescription or any special equipment and should be implemented for all patients in pain. A summary of the major options is as follows [29]:

- **Environmental**: Altering the environment such as temperature, bedding, body alignment, equipment and clothing.
- **Relaxation and guided imagery**: Such as focusing on one's breathing to control tachypnea or concentrating on a pleasant thought or scene. Meditation is also a form of relaxation. In guided imagery a trained practitioner reads or speaks in soothing tones whiles the patient focuses on a positive image. Relaxation and guided imagery are thought to counterbalance the "fight or flight" response the body often activates in response to pain. They can often reduce skeletal muscle tension, induce a decrease in vital signs, lower the metabolic rate and reduce oxygen consumption.
- **Cutaneous stimulation**: This focuses on non painful peripheral skin surfaces, thereby blocking the painful stimulation, causing a decrease in pain. Cutaneous stimulation techniques include massage, acupressure, acupuncture, hot and cold applications and transcutaneous electrical nerve stimulation (TENS).

Use of these non-pharmacologic interventions in addition to education and analgesics enhance the response to pain medication and help to alleviate the discomfort felt by patients.

2.2.8 Paediatric Analgesia

Pain in children: Pain perception mechanisms in infants and children and adults are similar. Pain may be even more intense in young infants because of differences in the nerve fibres involved in pain transmission and the modulation of pain in the spinal cord (30).

The main analgesic medications often found in paediatric analgesia are paracetamol and ibuprofen. In general, these drugs are safe and effective when used at their recommended doses (31). However, whether one would be more appropriate than the other would depend on the situation in which it is used.

Factors that need to be considered include the type of pain being treated, co morbidities and concomitant medication use (31). Because of its peripheral anti-inflammatory actions, ibuprofen is more effective than paracetamol for painful conditions associated with inflammation. Paracetamol does not reduce inflammation though it would decrease the pain associated with inflammation.

Comparative Studies: A meta-analysis of studies testing the efficacy and safety of single-dose acetaminophen and ibuprofen for treating children's pain or fever by Perrott et al showed that at recommended doses of 4-10 mg/kg of ibuprofen and 7-15 mg/kg of paracetamol, both drugs have similar efficacy for relieving moderate to severe pain with similar safeties as analgesics or antipyretics (32), however ibuprofen was shown to be a more effective antipyretic at regular dosing. Preparations combining both analgesics ostensibly to maximize analgesic and antipyretic effects can also be found on the local market and subsequently prescribed for various indications. The evidence

supporting the combination of paracetamol and NSAIDs in children are however conflicting (31).

Efficacy and Safety: Paracetamol is a safe medication when used at recommended doses, effective in mild to moderate pain, including musculoskeletal pain and pain associated with infections. The main potential harm is liver toxicity, but children are less susceptible to acute toxic effects as compared to adults. Rather they may be more susceptible to chronic exposure (31). Malnutrition, starvation and intercurrent febrile illness increase the risk of liver toxicity. Other risk factors include doses higher than 150 mg/kg, incorrect dosing in overweight children and use of cytochrome P450 enzyme inducing drugs such as phenobarbitone, phenytoin and rifampicin.

With ibuprofen, the NSAID related adverse effects are the same as for adults, however they seem to occur less often; though more frequently than paracetamol (33). The NSAID side effect of renal toxicity is increased with situations that are associated with decreased renal perfusion - dehydration, hypovolumoea and hypotension. A special group that is at increased risk of NSAID side-effects are children with NSAID-induced asthma. In a study conducted by Duplantier the prevalence of ibuprofen induced asthma in children with mild to moderate persistent asthma was found to be 2% (34).

2.2.9 Malaria and analgesia

Malaria is the number one reason for hospital outpatient attendance in Ghana [35]. Symptoms of this endemic tropical disease include fever, body aches and pain, headache, vomiting and poor appetite (36).

Pain in malaria thus consists of body aches and pains as well as headaches. The Standard Treatment Guidelines (2004) for the treatment of common conditions in Ghana recommends the use of paracetamol for the treatment of the pyrexia and pain associated with malaria especially in children (36).

Questions have been raised about the use of paracetamol in the treatment of especially *falciparum* malaria. .Brandts et al in a randomized trial in Gabon studied its effect on the parasite clearance time, recording that paracetamol significantly increased this (37). Matsiegue et al in a randomized, double blind placebo-controlled trial on the use of ibuprofen in malaria also in Gabon concluded that ibuprofen was effective in reducing the time a child is exposed to febrile temperatures, though its effect on fever clearance was not studied (38). Finally, Michael Sarrell et al (39) in a randomized, double blind, parallel group trial in central Israel on the antipyretic effects of the two medications in either a monotherapy or alternating regimen concluded that an alternating regimen of paracetamol and ibuprofen in the recommended doses every 4 hours for three days is more effective than monotherapy in reducing fever in young children.

CHAPTER THREE: METHOD

3.1 STUDY SETTING:

The Komfo Anokye Teaching Hospital (KATH) is a tertiary health care institution under the Ministry of Health, with specialist facilities and also teaching facilities to aid in the teaching of various health care professionals. Attached to the main hospital is a busy polyclinic which serves as first line institution for health care in the Kumasi metropolis in general and the surrounding communities in particular.

The polyclinic has ten outpatients consulting rooms. Consulting room one is for attending to KATH Staff and Staff of other institutions. Consulting room two is for paediatric cases. Consulting rooms three, four, seven and eight are for handling medical cases, room five for gynaecological cases, room six for anaesthetic assessment and two consulting rooms for trauma cases. Again at the polyclinic is a dental unit. There are also four wards at the polyclinic, two for surgical emergencies, male and female, one for medical emergencies and the other one for medical recovery. For the purposes of this study, prescriptions from the general consulting rooms, ie rooms one, two, three, four, seven and eight were surveyed.

Prescriptions and medication requests from all these areas are normally sent to the polyclinic pharmacy as a first point of call by outpatients, patient carers and nurses. The pharmacy supplies whatever medications are available, referring any unavailable prescriptions to pharmacies outside the hospital. With the advent of the National Health Insurance scheme, the pharmacy has subsequently been divided into two serving areas:

one for paying patients and one for patients registered under the health insurance scheme. Both pharmacies run a 24 hour schedule.

3.2 METHOD:

Study type: A descriptive prospective cross-sectional study was carried out over a period of four weeks from mid – December 2006 to mid - January 2007.

Ethical clearance: This was sought from the Committee on Human Research, Publications and Ethics of the School of Medical Sciences, KNUST. (Appendix B)

Sampling: A purposeful sampling method was employed. Both serving areas of the pharmacy were surveyed and all prescriptions coming to both areas were analyzed for analgesic orders. Twenty consecutive prescriptions containing analgesics were picked each day that sampling was done and details recorded using the data collection tool attached as appendix A.

Pilot Study: The questionnaire was pre-tested using twenty prescriptions. Two Dispensary Technicians were trained on the study and the data collection. After this, the actual data collection was carried out.

Data Collection Tool: The data collection tool employed is attached as Appendix A. A table was laid out with the various parameters to be analysed in each column. The first three columns on data sheet A sought to collect data about each patients identity – age and sex as well as the diagnosis as recorded at the consulting room. These sought to answer objectives 1 and 2. The next four columns looked at the analgesic prescription itself, the analgesic, its class, dose and duration of therapy. On sheet B, general patterns were looked at: generic prescribing, whether the therapy was indicated for the diagnosis

recorded availability at the pharmacy and if it was on the Drugs and therapeutic Committee list. These sought to answer objectives 3 to 5.

Data Collection: Each day (apart from weekends and public holidays), prescriptions from the morning and afternoon shifts were selected as and when presented at the counters over a period of four weeks. The first twenty prescriptions containing any analgesics were included and record taken of all analgesics prescribed. Two dispensers, one on each shift in both areas were assigned the duty of screening the prescriptions as they were presented. Patient particulars on the prescriptions were also recorded and followed up to the consulting rooms where record books of presenting complaints and other particulars were kept. Prescribers and patients were not interviewed in order not to bias the prescribing pattern.

Inclusion criteria: Prescriptions from the general consulting rooms, ie rooms one, two, three, four, seven and eight only were surveyed.

Exclusion criteria: Prescriptions which did not contain any analgesic drugs were excluded from this study. Adjuvants to analgesic therapy were also not included in this survey.

Data Processing and Analysis: Numbers and percentages were calculated using the electronic data processing software SPSS (version 12).

Limitations of the study: This study had some limitations. Firstly, the time period used for the study was relatively short and thus the data collected may not necessarily reflect the overall prescribing patterns throughout the year. As only current prescriptions were analyzed, previous and future prescribing sequences could not also be effectively commented upon.

CHAPTER FOUR: RESULTS

Three hundred and forty prescription forms were analyzed from the outpatients' pharmacies. There were a total of three hundred and sixty-nine analgesic prescriptions on these.

4.1 DEMOGRAPHIC CHARACTERISTICS

- Sex Distribution:

A total of 65.4% of all prescriptions were for females whiles 34.6% were for males (Fig. 4.1). Of all prescriptions analyzed for children under five years however, more were for males (62.7%) than females (37.3%) (Fig 4.2), whiles in the age group over 14 years however, females formed the larger group of 73.4% and males were 26.2% (Fig 4.3).

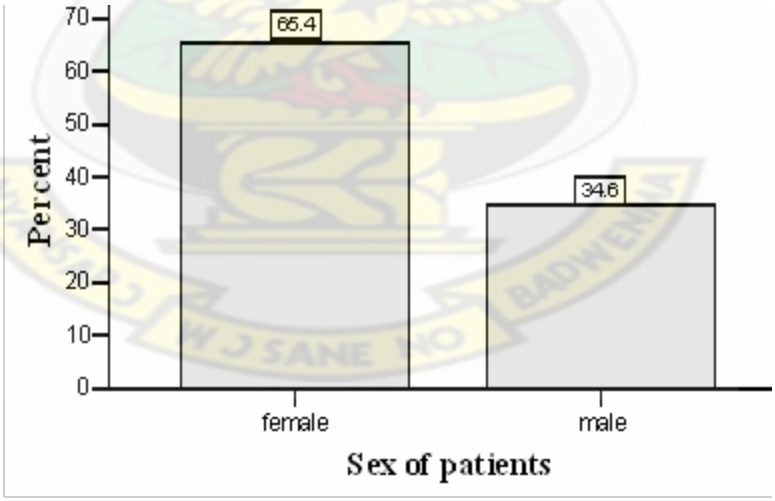

Figure 4.1: Sex distribution of all patients

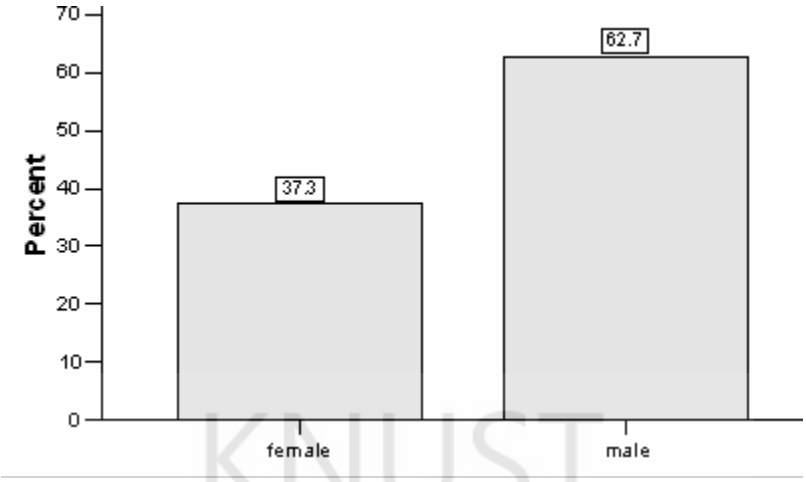

Figure 4.2: Sex distribution of patients under five years

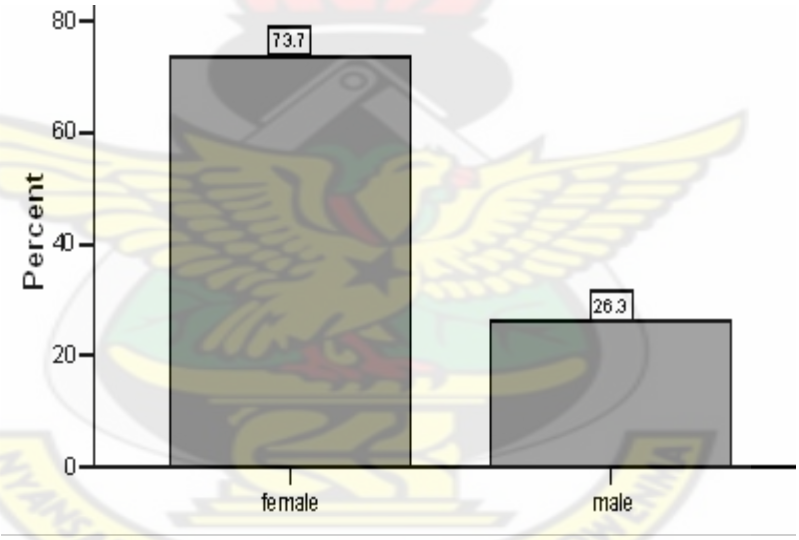

Figure 4.3: Sex Distribution in all age groups over 14 years

-Age Distribution:

The largest proportion of all analgesic prescriptions went to the age group 15-45 years (34.1%). This was followed by the 45-65 years group (23.3%) (Fig 4.4)

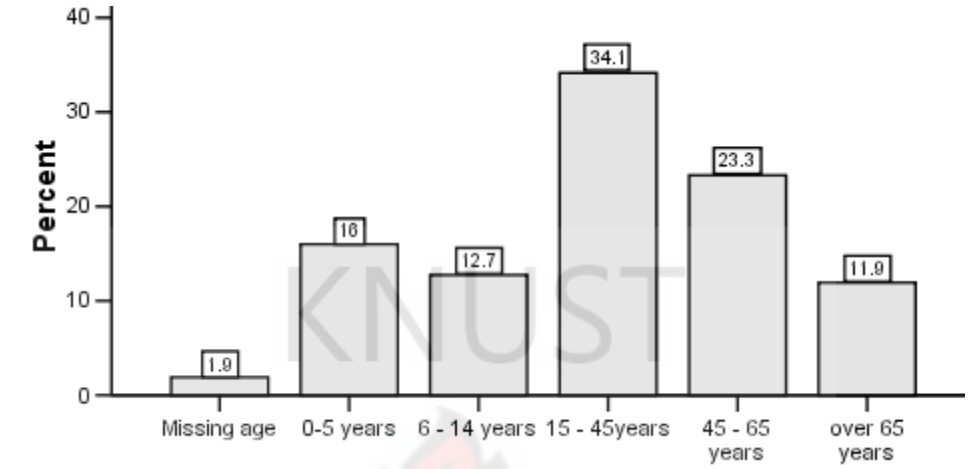

Figure 4.4: Age distribution

4.2 CONDITIONS FOR WHICH ANALGESICS WERE PRESCRIBED

A total of forty different primary diagnoses were recorded for which analgesics were prescribed (Table 4.1.). Of these, 23.8% also had a second diagnosis. No diagnoses at all were recorded for nine cases (2.4%). Overall, malaria was the commonest indication (51.8%) (Table 4.1).

TABLE 4.1: PRIMARY DIAGNOSES FOR WHICH ANALGESICS PRESCRIBED

	Frequency	Percent
anxiety	2	.5
appendicitis	1	.3
arthritis	2	.5
asthma	1	.3
back ache	1	.3
chest pain	1	.3
CVA	3	.8
cystitis	2	.5
diabetes	1	.3
dog-bite	3	.8
dysentery	1	.3
enteritis	9	2.4
epidydimis ochitis	1	.3
erypsela	1	.3
facial palsy	1	.3
fibroids	1	.3
gastritis	3	.8
GERD	1	.3
HIV	3	.8
hypertension	63	17.1
inguinal hernia	1	.3
malaria	191	51.8
menopause	2	.5
migraine	1	.3
myalgia	10	2.7
No record	9	2.4
osterculosis	2	.5
pautidity	1	.3
pelvic mass	1	.3
peptic ulcer	5	1.4
pneumonia	4	1.1
pyelonephritis	5	1.4
rhinitis	4	1.1
sciatica	3	.8
sickle cell	2	.5
sinusitis	3	.8
STD	1	.3
tonsilitis	2	.5
tuberculosis	1	.3
URTI	16	4.3
UTI	4	1.1
Total	369	100.0

In the age groups, malaria was the commonest indication in the age groups under 5 years (83.1%) (Fig 4.5), but hypertension was the commonest indication in the age groups 45-65 years (41.9%) and over 65 years (45.2%) (Fig 4.6)

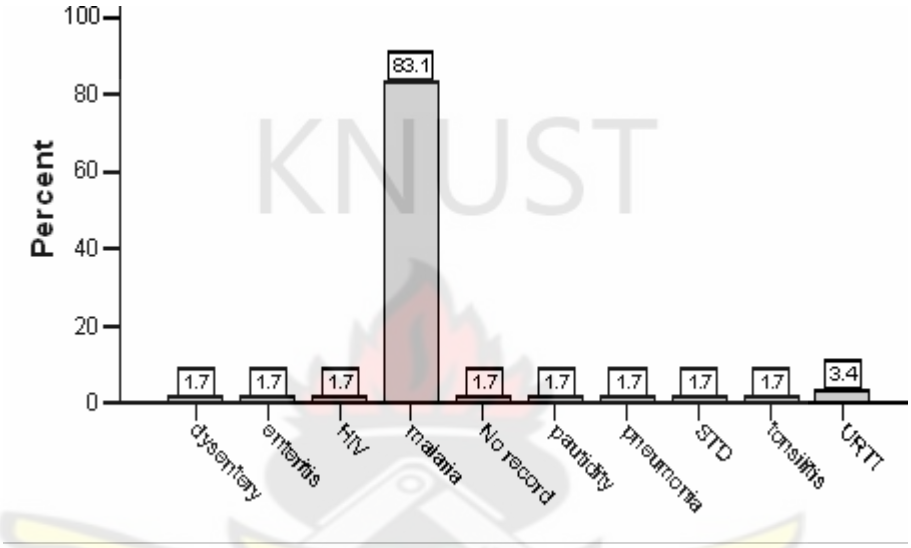

Figure 4.5: Primary diagnosis recorded for patients under five years

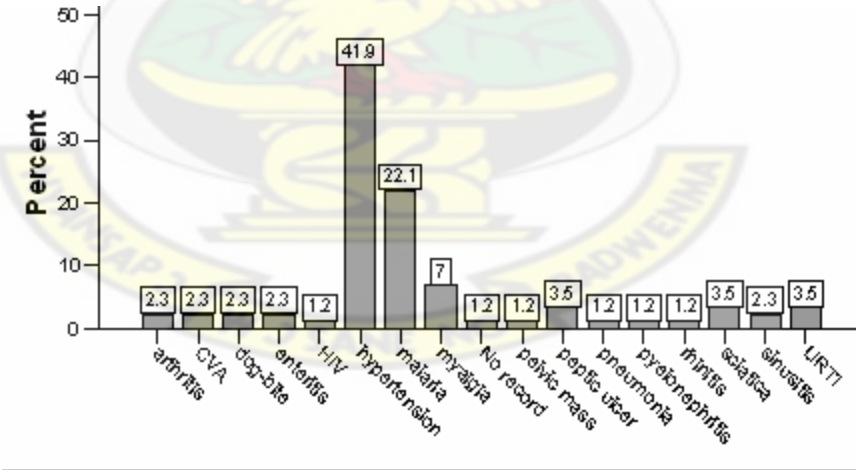

Figure 4.6: Primary Diagnosis recorded for patients 45 – 65 years

4.3 ANALGESIC PRESCRIBING PATTERNS

The most commonly prescribed analgesic class was paracetamol (non-opioid) (52.8%) whiles NSAIDS followed at 40.1% (Fig 4.7). Of the individual NSAIDS, diclofenac was most commonly prescribed in various forms (68.9%) (Fig. 4.8). As a whole, paracetamol was the most prescribed individual analgesic drug (Table 4.2).

TABLE 4.2: ANALGESICS PRESCRIBED

	Frequency	Percent
aspirin	2	.5
celecoxib	4	1.1
dexfin	1	.3
diclofenac	82	22.2
diclofenac gel	21	5.7
dihydrocodeine	1	.3
doloneurobion	2	.5
ibuprofen	29	7.9
naprosyn	4	1.1
nimesulide	6	1.6
optalidon	1	.3
paracetamol	194	52.6
parafen forte	11	3.0
pethidine	1	.3
sedadouzabox	1	.3
tramadol	9	2.4
Total	369	100.0

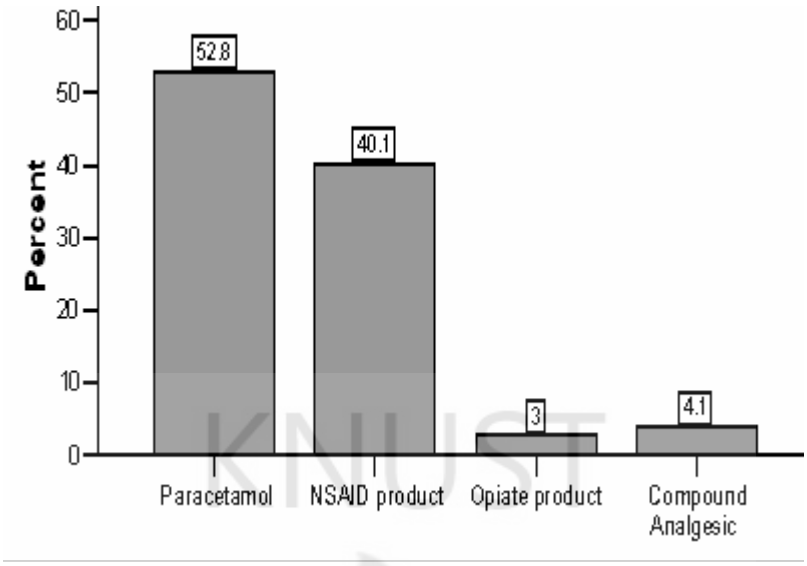

Figure 4.7: Class of analgesics prescribed

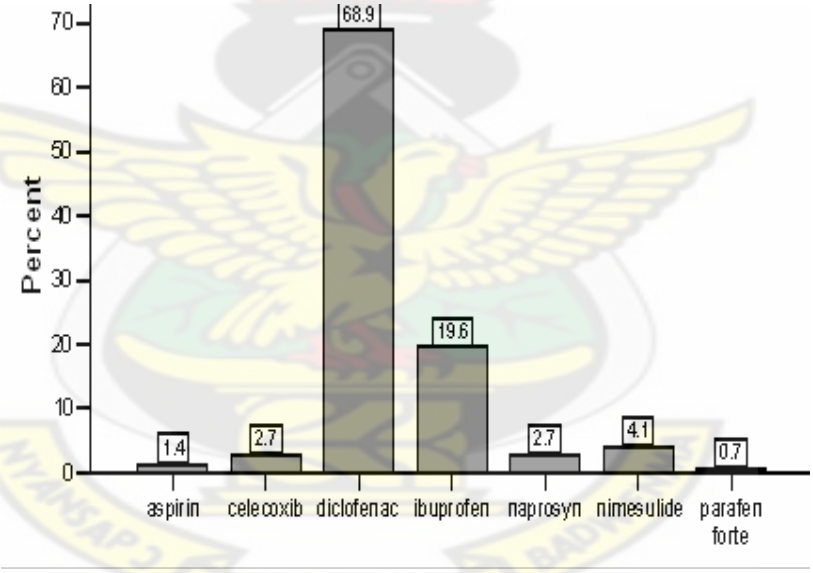

Figure 4.8: Types of NSAIDs prescribed

NSAID use:

As a class, NSAIDS were primarily used in malaria (34.5%), followed by use in hypertension (25%) (Table 4.3). In the various age groups, NSAID use was highest in

the age group 15-45 years (43.2%), followed by the group 45-65 years (37.2%) (Fig 4.9).

TABLE 4.3: PRIMARY DIAGNOSES IN WHICH NSAIDS WERE PRESCRIBED

	Frequency	Percent
anxiety	2	1.4
arthritis	1	.7
back ache	1	.7
chest pain	1	.7
CVA	1	.7
cystitis	1	.7
dog-bite	2	1.4
enteritis	1	.7
epidydimis ochitis	1	.7
facial palsy	1	.7
fibroids	1	.7
GERD	1	.7
HIV	2	1.4
hypertension	37	25.0
malaria	51	34.5
migraine	1	.7
myalgia	8	5.4
No record	5	3.4
osterculosis	1	.7
pautidity	1	.7
pelvic mass	1	.7
peptic ulcer	1	.7
pneumonia	2	1.4
pyelonephritis	3	2.0
rhinitis	3	2.0
sciatica	2	1.4
sickle cell	1	.7
sinusitis	2	1.4
STD	1	.7
URTI	9	6.1
UTI	3	2.0
Total	148	100.0

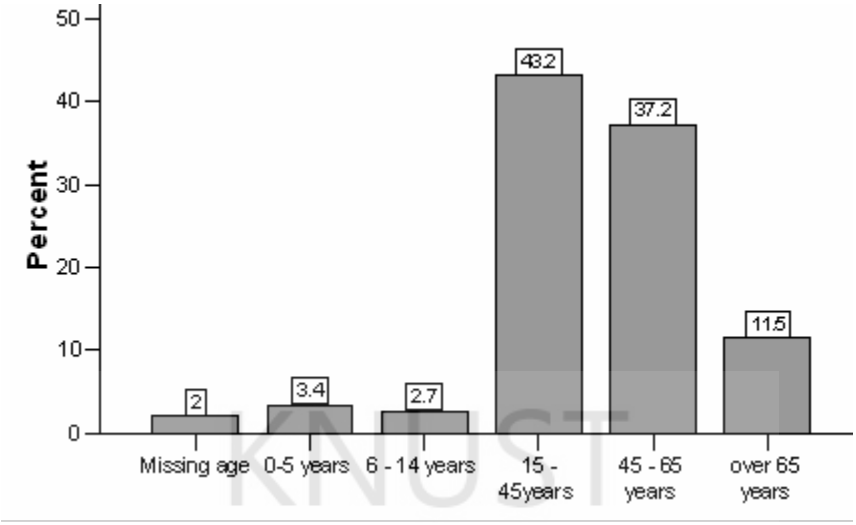

Figure 4.9: Age distribution of NSAID use

Analgesic use and malaria:

In all the cases where a primary diagnosis of malaria was recorded, paracetamol was the major analgesic used (67.5%). NSAIDS followed at 26.7% (Fig 4.10). The mean duration of therapy of paracetamol in malaria for children under five was 5 days (Table 4.4). Where the only diagnosis recorded was malaria with no other diagnosis, in all age groups over 14 years, paracetamol was still the major analgesic (48.4%) but NSAID use followed closely at 41.9% (Fig 4.11).

TABLE 4.4: MEAN DURATION OF PARACETAMOL THERAPY IN UNDER FIVES

	N	Minimum	Maximum	Mean
Duration of therapy	46	2	7	5.00
Valid N (listwise)	46			

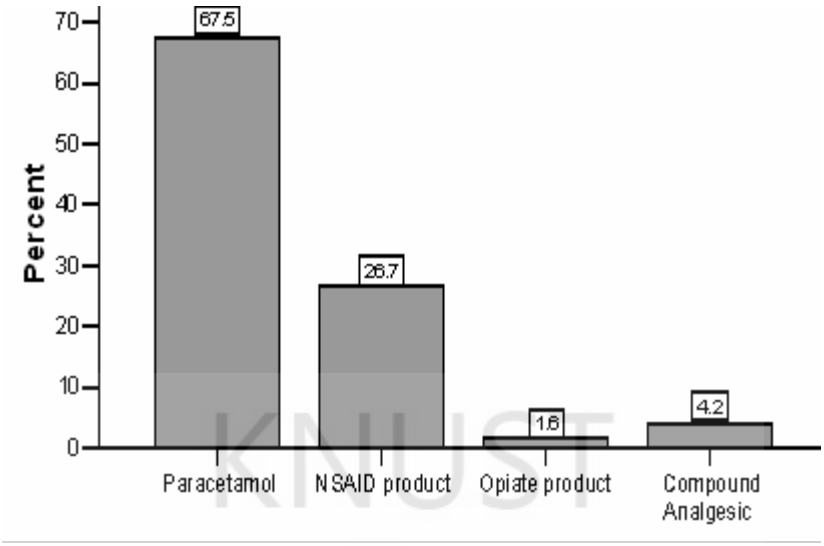

Figure 4.10: Analgesic prescription in Malaria

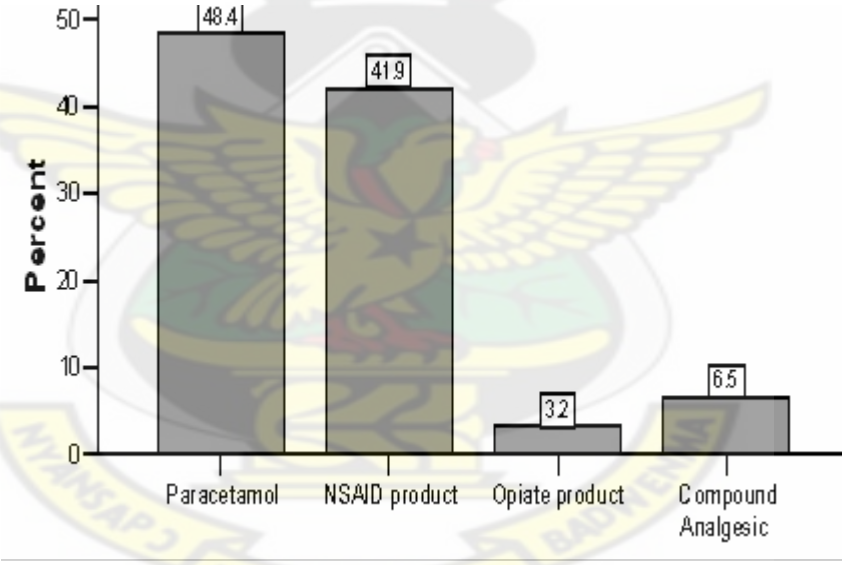

Figure 4.11: Analgesic use in malaria with no second diagnosis (Over 14 years)

Analgesic use for hypertensives:

A look was also taken at trend of prescribing for patients whose primary diagnosis was recorded as "hypertension". Of all these cases, the majority received NSAIDS (58.7%) whiles 36.5% received paracetamol (Fig 4.12). Only a small proportion of such records

also had a second diagnosis obviously requiring some analgesia (myalgia-7.9% and malaria 3.2%) (Fig 4.13). In all cases of hypertension as a primary diagnosis with no other recorded complaint, most patients received NSAIDS (59.3%) (Fig 4.14).

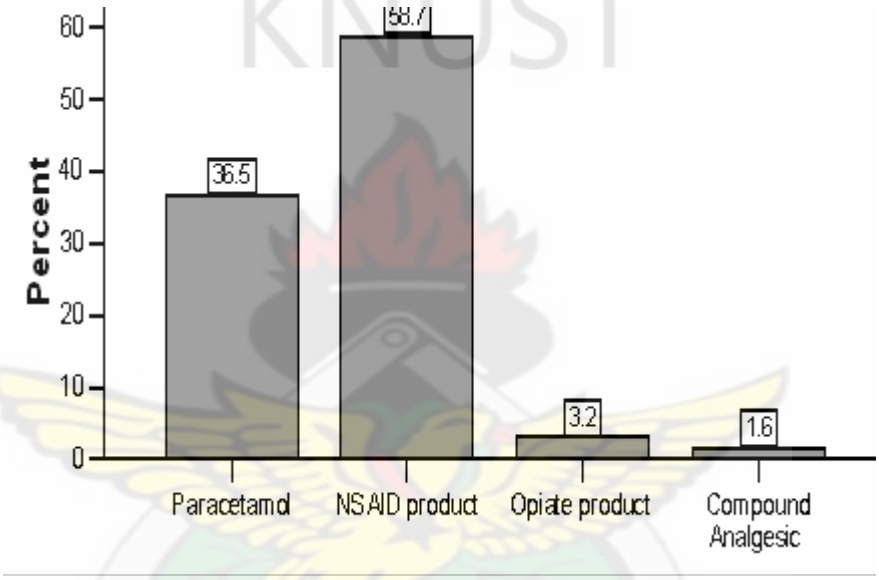

Figure 4.12: Analgesic use in diagnosis of Hypertension

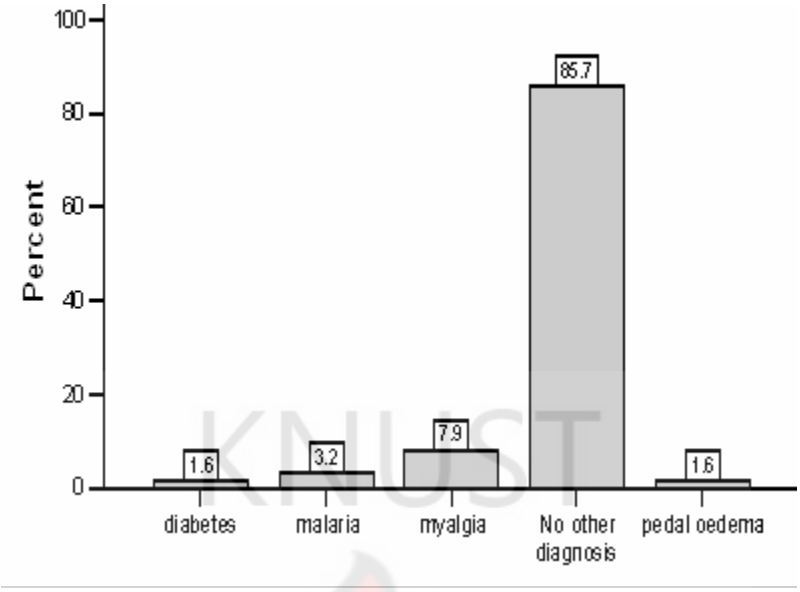

Figure 4.13: Hypertension recorded with second diagnosis or no diagnosis

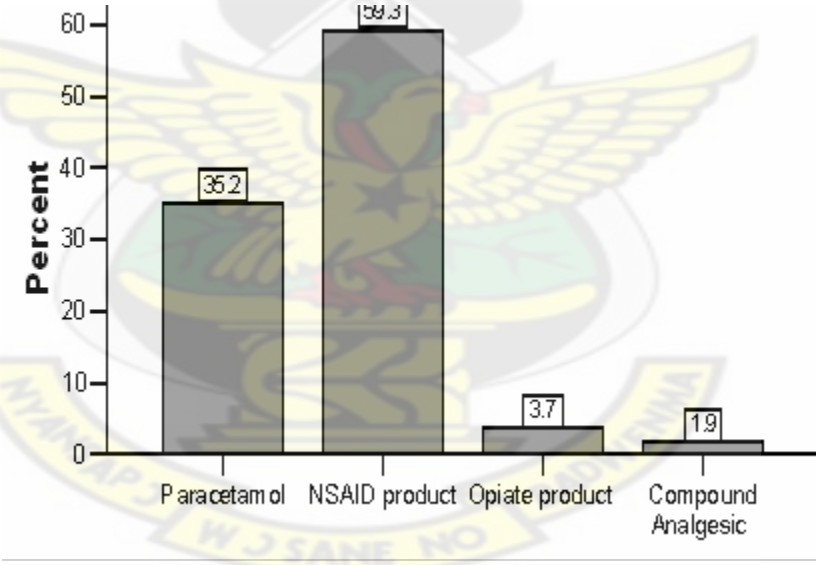

Figure 4.14: Class of analgesic prescribed for patients with hypertension but no other recorded diagnosis

4.4 GENERIC PRESCRIBING AND AVAILABILITY

Overall, the trend was mostly to prescribe generically (79.1%) (Fig.4.15)

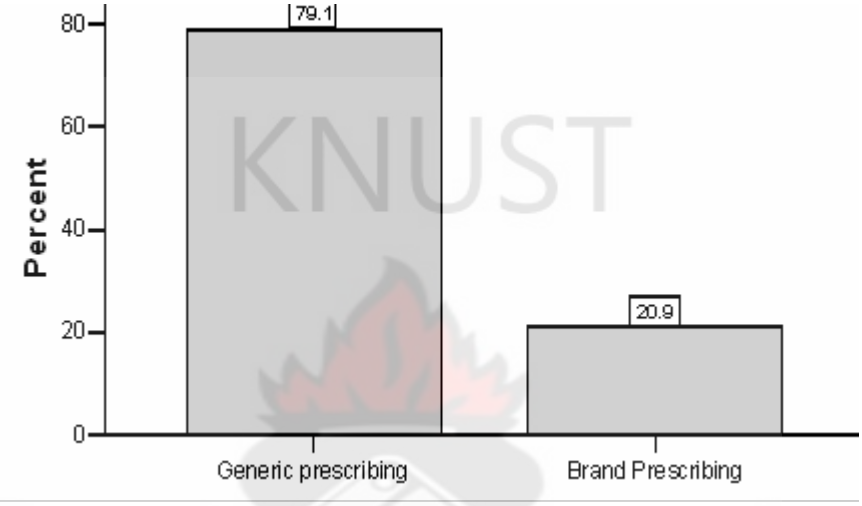

Figure 4.15: Generic Prescribing

Diclofenac was the analgesic most prescribed by brand name (37.3%) followed by ibuprofen (22.9%) (Fig 4.16). Most analgesics prescribed were available at the pharmacy (95.7%) (Fig. 4.17). Sixteen drugs were not available, of which nimesulide was the most prescribed (37.5%) (Fig 4.18).

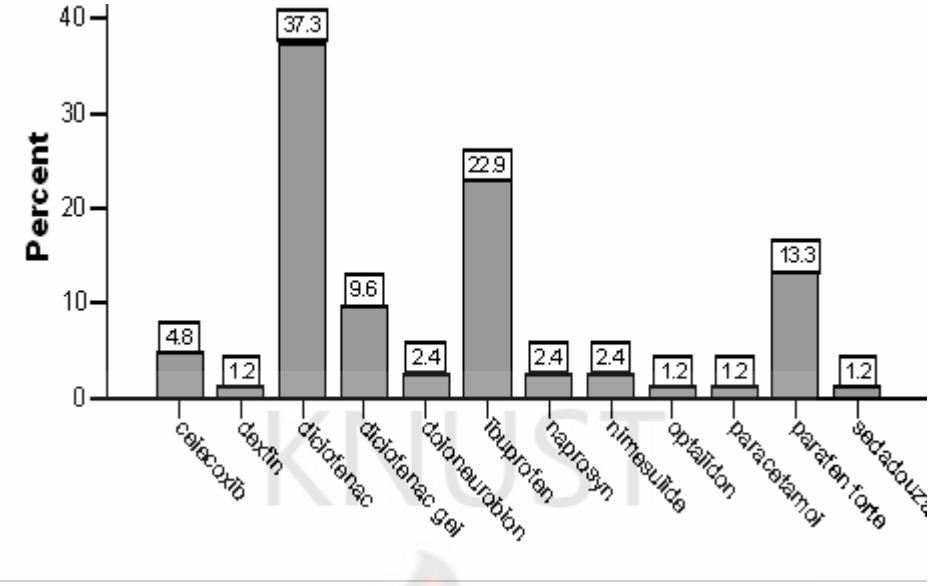

Figure 4.16: Drugs prescribed by brand name

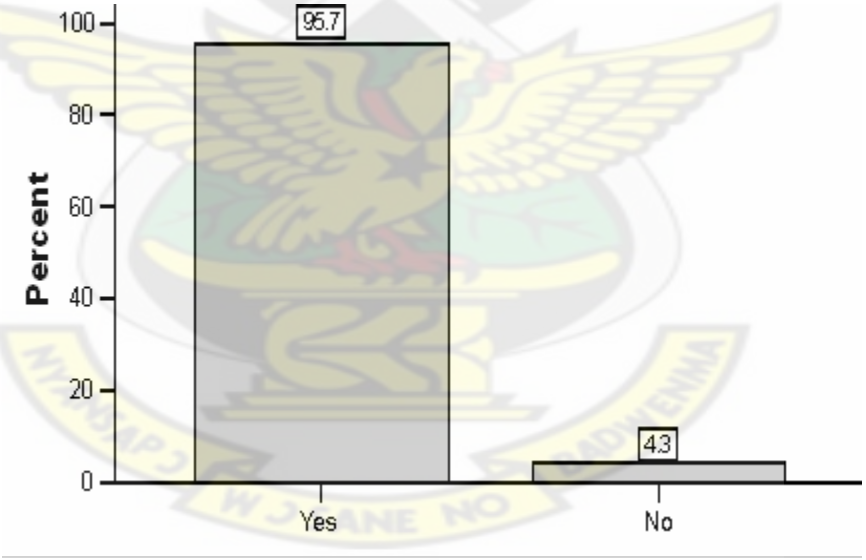

Figure 4.17: Availability in the pharmacy

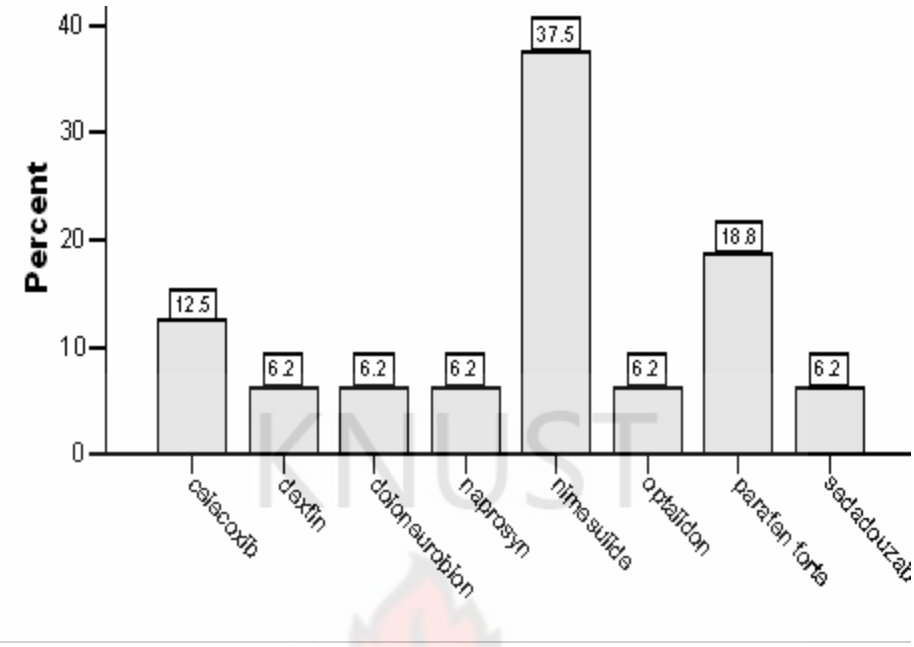

Figure 4.18: Analgesics not supplied by pharmacy

4.5 APPROPRIATENESS OF ANALGESIC PRESCRIPTIONS:

The analgesic prescribed was matched with the individual diagnosis recorded. Though many conditions require the use of analgesics to alleviate the discomfort of pain, prescribing NSAIDS alone in malaria or hypertension with no other recorded complaint was considered inappropriate. Using this criterion, 72.1% of analgesic prescriptions were considered appropriate (Fig 4.19).

Of the 25.5% considered inappropriate, the majority (46.9%) was in malaria, followed by hypertension (36.7%) (Fig. 4.20). This group included the use of purely NSAID products in malaria, prescribing NSAIDs with a diagnosis of only hypertension, in recognized peptic ulcer disease and respiratory tract infections, bearing in mind the negative effects of these analgesics in these cases. There were no recorded diagnoses in nine cases (2.4%).

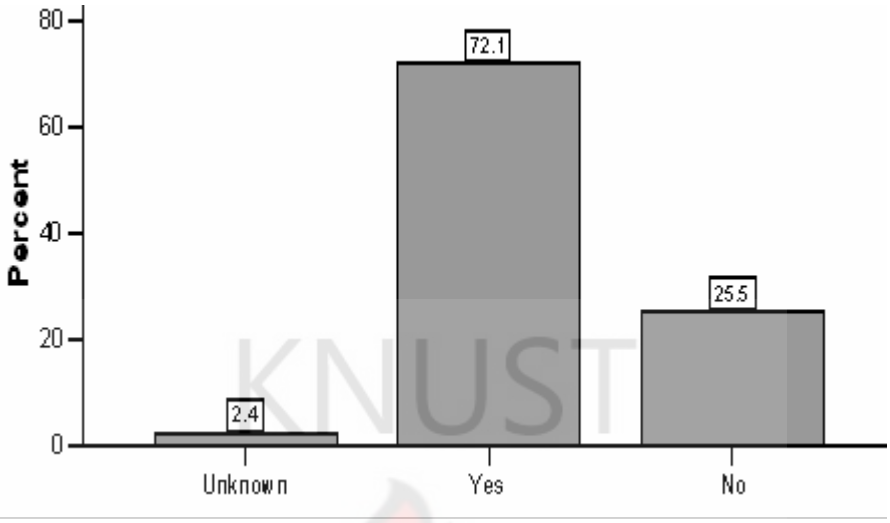

Figure 4.19: Appropriateness of analgesic prescribed to condition

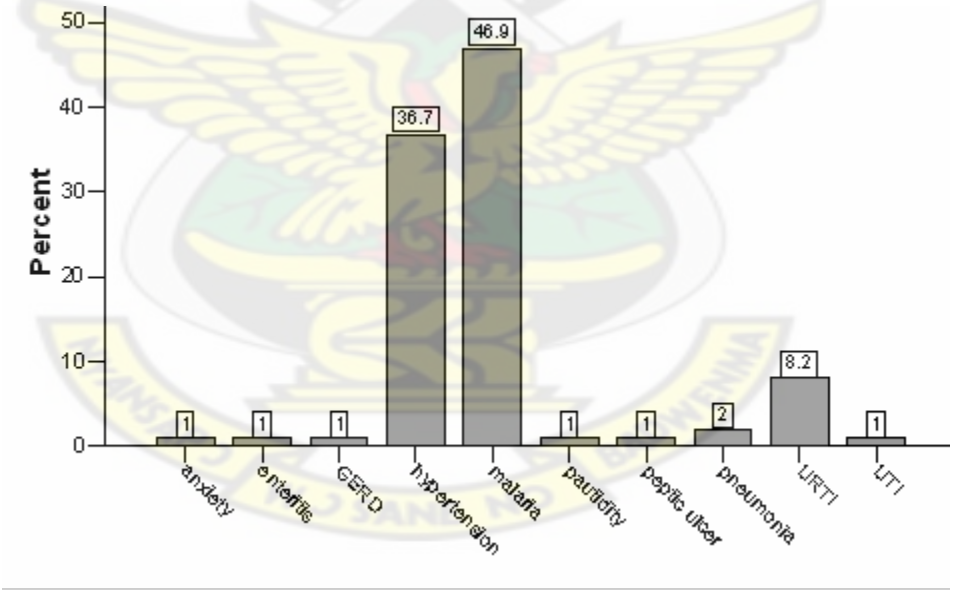

Figure 4.20: Use of NSAIDs considered inappropriate

4.6 ADHERENCE TO DRUG AND THERAPEUTIC COMMITTEE LIST

Most of the analgesics prescribed were on the hospital's DTC list (94.3%) (Fig. 4.21).

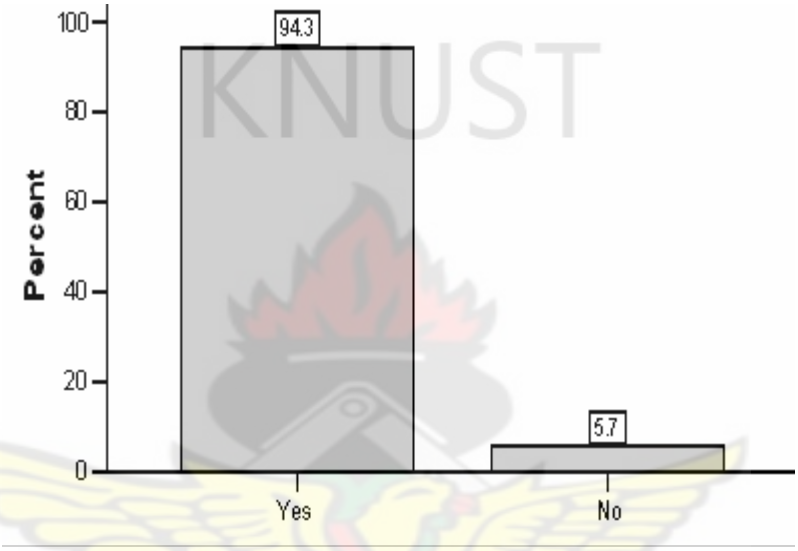

Figure 4.21: Percentage on approved list

CHAPTER FIVE: DISCUSSION

This study set out to look at the way analgesics are prescribed in a busy primary health care facility in the light of the common perception that they are frequently prescribed in cases where they may not necessarily be needed.

Paracetamol was found to be generally the most prescribed analgesic, accounting for 52.6% of all analgesic prescriptions. This finding correlates well with the finding of malaria being the most documented diagnosis (51.8%). Paracetamol has well documented antipyretic properties which have made it an accepted adjuvant in the treatment of malaria, which has pyrexia as a major symptom (36).In a study by Rahman et al in Bangladesh, a similar pattern where paracetamol and other similar agents formed the larger percentage of analgesics prescribed in the OPDs of two major teaching hospitals was reported (40). Also, co-prescription of analgesics with antimalarials was shown to be common in a study in Benin City, Nigeria by Akoria, Isah et al (where 82.1% of all antimalarial prescriptions also had an analgesic) (41).

The mean duration of paracetamol therapy prescribed for malaria in children was found to be five days. There have been some questions on the effect of paracetamol on the duration of malaria in children, especially on parasite clearance (37). Though conclusive evidence on this is yet to be established, reducing the mean number of days antipyretics are given in favor of mechanical methods of antipyresis may be well beneficial. Shanks et al cautioned on the repeated dosing of paracetamol in children either within the normal therapeutic range or at doses slightly higher, in view of recorded cases of adverse effects, including death (42).

In the age group 0-5 years, the male sex was dominant (62.7%). Malaria was the major diagnosis in this group and other studies elsewhere in Africa have also documented the predominance of male children (43). Schellenberg, in a study from Tanzania postulate that this may be due to male children culturally being cared for better than females across malaria endemic areas - mostly in developing countries (44).

The most frequently recorded diagnosis after malaria for which NSAIDs were prescribed was hypertension. The age group of 45-65 years accounted for the most use of NSAIDS in hypertension. Whiles it may be argued that in this aging population, there will be a higher incidence of musculoskeletal complaints requiring the use of NSAIDs; this is not indicated in the study results. As Ghana is a developing country with a relatively low life expectancy- 56 years for men and 58 years for women (WHO 2005)(45), the high incidence of NSAID prescriptions in older ages could give some cause for concern. Results of various studies have linked the use of NSAIDs to the initiation of antihypertensive therapy in older persons (46). A meta-analysis of randomized trials studying the effect of NSAIDS on blood pressure showed that they may elevate blood pressure and antagonize the BP lowering effect of antihypertensive medications to an extent that may potentially increase hypertension related morbidity (47). In the study by Desta et al in Ethiopia, one conclusion drawn was the seemingly overuse of analgesics with their prescribing frequency not correlating with available morbidity data (3).

In the sample size selected, women generally formed the larger percentage (65.4%). This trend was even more obvious when the population is separated into only ages over 14 years, rising to 73.4%.In the study by Truter in South Africa on NSAID use, the same result was found (4). Some reasons which may be assigned to this include the relatively

higher life expectancy of Ghanaian women than men as stated above, and the finding that women generally tend to feel pain more. This latter finding is a conclusion from a study by researchers from the Pain Management Unit at the University of Bath, UK (48). This, if also true across all populations will obviously result in more women reporting at the clinic.

The high rate of generic prescribing at the polyclinic is commendable and is in line with national prescribing guidelines (49). Availability of prescribed products at the pharmacy was also generally good at 97%. This demonstrated a high awareness of doctors of the drugs on the Drugs and Therapeutic Committee's approved list. Again, 95% of all products prescribed were on the DTC list. An examination of the appropriateness of the analgesic to diagnosis recorded showed that 72.1% was satisfactory, whiles 25.5% were regarded doubtful. This group included the use of purely NSAID products in malaria, prescribing NSAIDs with a diagnosis of only hypertension, in recognized peptic ulcer disease and respiratory tract infections, bearing in mind the negative effects of these analgesics in these cases.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION: Analgesic use was found to be closely correlated to the pattern of malaria diagnosis at the polyclinic, especially in younger age group below 45 years. Visits related to hypertension accounted for most of the diagnoses in the age groups above 65 years, with no clear indications for analgesic usage. Paracetamol was the most commonly prescribed medication, followed by NSAIDs especially diclofenac. Paracetamol was also mostly used for malaria, with a mean duration of therapy being 5 days. However, NSAID use was more common in the middle age group of 45-65 years, being used in most diagnoses ranging from malaria through hypertension to various infections. Most analgesics prescribed were on the Hospital's approved list, and most analgesics were supplied at the pharmacy.

6.2 RECOMMENDATIONS:

1. Feedback to prescribers about the tendency to use NSAIDs in the older age group should be given so that as much as possible the use is restricted to clearly diagnosed cases requiring analgesia.

2. The hospital would benefit from a special pain clinic for especially older patients with chronic pain, which would explore non-pharmacological means of dealing with pain.

3. A standardized fever and pain reduction protocol may be needed in the treatment of malaria in the light of studies on the effect of paracetamol on malaria parasite clearance, especially in children; probably favoring mechanical means over aggressive pharmacological methods.

4. Further in depth studies on the use of NSAIDs in the identified age group of 14-65 years will be beneficial in identifying any irrational trends in analgesic prescribing which need to be curtailed.

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APPENDICES

APPENDIX A: DATA COLLECTION TOOL

DATA COLLECTION TOOL (A)

DATE:.....

Serial	Patient ID	Patient Age	Patient Sex	Diagnosis	Drug	Class	Dose	Duration

DATA COLLECTION TOOL (B)

DATE:.....

Serial	Patient ID	Generic YES/NO	Indicated YES/NO	Supplied by Pharmacy YES/NO	Approved by DTC YES/NO	Comments	

APPENDIX B

ETHICAL APPROVAL

COMMITTEE ON HUMAN RESEARCH PUBLICATION AND ETHICS
KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICAL SCIENCES - KATH

November 6, 2006.

CHRPE/10/12/06

Prof. Mahama Duwlejua
Clinical and Social Pharmacy
KNUST

Dear Sir,

TITLE: ANALGESICS USE AT POLYCLINIC OPD, KATH

Your application for Ethical Committee clearance for the study "*Analgesics Use at Polyclinic OPD, KATH*" has been considered and approved by the Committee on Human Research, Publication and Ethics (CHRPE) of the School of Medical Sciences, Kwame Nkrumah University of Science and Technology, Kumasi and the Komfo Anokye Teaching Hospital, Kumasi.

The Committee recommends that samples and or materials taken for this study should be used for the study only. Any subsequent use of the samples for other studies will need clearance from the CHRPE.

The Committee also recommends that it should be informed of any adverse events; it would therefore expect a periodic report of your study to the committee. Its permission should be sought for any amendments to the protocol. The Committee should be informed of all publications arising from the study and copies of the same should be sent to the committee.

Professor Sir J. W. Acheampong, MD, FWACP
Chairman

Private Mail Bag, University Post Office, Kumasi, Ghana. Phone: 233-51-60303/60294. Fax 233-51-60302.
E-mail: secretary.sms@knust.edu.gh website: www.knust.edu.gh