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Comparative Study to Assess the Effectiveness and Safety of Etoricoxib & Aceclofenac in Osteoarthritis Patients

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Abstract **Original Research Article**

Osteoarthritis (OA) is defined as a disorder that involves the movement of limbs characterized by cellular stress and a deterioration of the outer matrix that trigger malignant remodelling responses that include inflammatory mechanisms of natural immunity. Non-steroidal anti-inflammatory (NSAID) drugs are the first choice of treatment, since they reduce pain, improve functional ability. So, by comparing the effectiveness and safety of NSAID used in the treatment of OA can enhance the quality of life of patients. The goal of the study was to compare the effectiveness and safety of Aceclofenac and Etoricoxib in OA patients as well as to assess the quality of life (QOL) and medication adherence among subjects. It is an observational study conducted in the selected Orthopaedics clinics in T. Dasarahalli, Bengaluru District for a period of 6 months, based on various inclusion and exclusion criteria. Standardized questionnaire used in the study were Western Ontario and McMaster Universities Arthritis Index, Medical Outcomes Study 36-Item Short-Form Health Survey and Morisky Medication-Taking Adherence Scale. The collected data were entered in Microsoft Excel and appropriate descriptive and inferential statistical analysis was performed. On comparing Aceclofenac and Etoricoxib in terms of WOMAC score Etoricoxib (28.42) was found to be more effective than Aceclofenac (31.61) while comparing Etoricoxib 60 mg and 90mg, 90 mg (26.22) was found to be more effective. Regarding the safety of these drugs, Etoricoxib was found to be safer than Aceclofenac in terms of side effects. On associating the QOL scores in both the groups, it was found that the subjects belonging to the Aceclofenac group had the highest overall mean score 57.68. Investigation of medication adherence in the study population revealed that out of 68 subject's majority of them had shown low adherence (n=38). Because of its enhanced safety profile, Etoricoxib is a better option than Aceclofenac for treating osteoarthritis symptoms.

Keywords: Aceclofenac, Etoricoxib, Osteoarthritis, WOMAC, HRQOL, MMAS-4.

INTRODUCTION

Osteoarthritis (OA), a chronic degenerative ailment marked by cartilage loss, is a diverse condition. It is a significant contributor to disability and is exceedingly pervasive in society. Although nodal deformities of the interphalangeal joints have intrigued some people since the early 18th century and the name osteoarthritis implicitly acknowledges that inflammation plays a role in the presentation, little else has been done to distinguish osteoarthritis from other types of arthritis. One of the most typical musculoskeletal conditions reported in all nations around the world is osteoarthritis. It is the ninth most frequent predictor of ill health in men and the fourth most frequent predictor of health problems in women worldwide [2-5]. The condition imposes a significant strain, with significant repercussions for affected individuals, healthcare systems, and broader socioeconomic consequences [6]. Hip and knee OA account for a significant amount of the strain of OA, which may eventually require joint replacement [7].

According to the Global Burden of Disease (GBD) study, the number of persons suffering from osteoarthritis (OA) has increased significantly since 1990. OA rated 19th in terms of age standardized prevalence rates (ASRs) and 17th in terms of the prevalence of cases among 369 diseases and injuries examined in the GBD 2019 survey. The frequency rises

with age, is much more prevalent in women (51%) than in men (33.09%), is more prevalent in those with higher body mass index (BMI) and in urban settings than in rural ones. Women who have undergone menopause are more affected than those who have not, it was discovered that homemakers had a greater rate than professionals [8, 9]. The aetiology of OA is multifactorial and involves factors such as joint damage, obesity, ageing, and inheritance. Early stages of OA entail increased cell proliferation and chondrocyte manufacture of matrix proteins, proteinases, growth factors, cytokines, and other inflammatory mediators. Chondrocyte is the key cellular mediator of OA pathogenesis it is further aided by the synovium and subchondral bone, two additional cells and tissues of the joint [10, 11].

The most prevalent subgroup of the disease, primary OA, is diagnosed without a preceding injury or illness but is linked to the risk factors. Primary OA is brought on by aging-related joint wear and tear. As a consequence, it starts to show up in persons between the ages of 55 and 60. Although cartilage degeneration is a universal problem with ageing, certain cases are more severe than others. When a joint problem already exists, secondary OA develops. Among the risk factors include trauma or injury, congenital joint diseases, infectious arthritis, inflammatory arthritis, avascular necrosis, Paget disease, osteopetrosis, osteochondritis dissecans, hemoglobinopathy, Ehlers-Danlos syndrome, and Marfan syndrome. Secondary OA is caused by a specific trigger that exacerbates cartilage degradation, these are a few [12, 13].

Osteoarthritis is primarily diagnosed through detailed medical history and physical exam findings, either with or without radiographic support. The most typical symptom, even if some people may initially show no symptoms, is pain. If the following conditions exist, it is possible to confidently identify OA as a clinical diagnosis: 1) older than 45 years old, 2) stiffness in the morning lasting less than 30 minutes, 3) more than an hour to an hour worth of morning stiffness, 4) bony joint enlargement, 5) limits to range of motion. Among other soft tissue abnormalities, the differential diagnosis should incorporate rheumatoid arthritis, psoriatic arthritis, crystalline arthritis, hemochromatosis, bursitis, avascular necrosis, tendinitis, and radiculopathy into care. On radiographs, OA can be seen as joint space narrowing, osteophyte formation, subchondral sclerosis, and subchondral cysts [12, 14, 15].

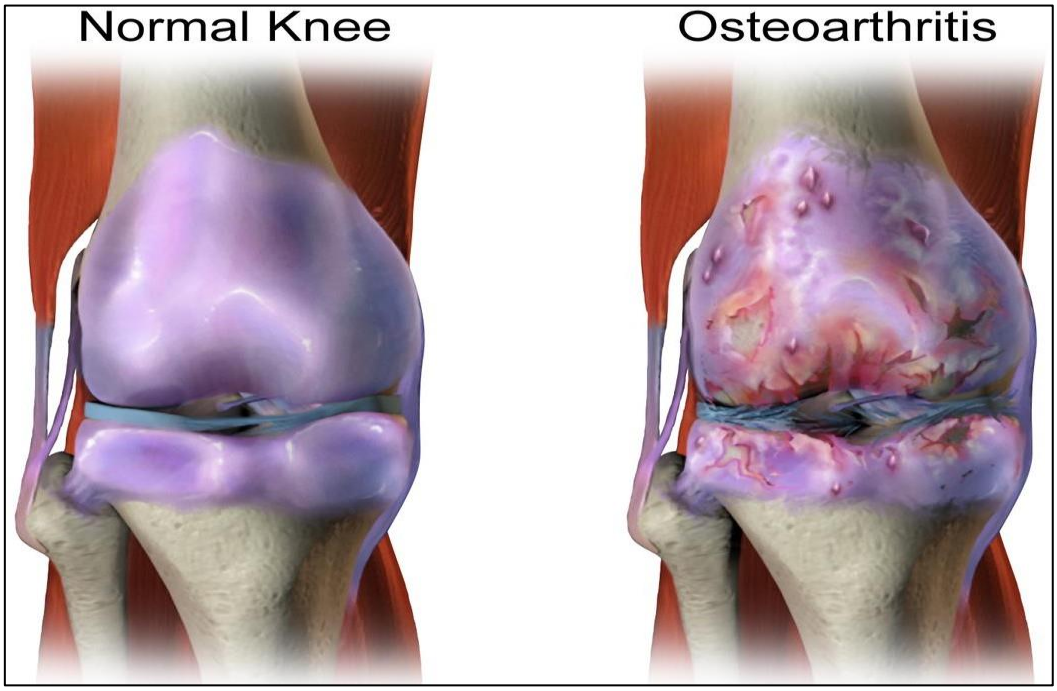


Figure 1: The difference between healthy joint and Osteoarthritis [1]

Table 1: Risk Factor for OA [15, 16]

Modifiable	Non-modifiable
• Arthritic injury	• Females are more prevalent than males
• Long-standing work that requires frequent knee bending	• Age
• Muscle sluggishness or imbalance	• Genetics
• The metabolic syndrome and weight	• Race
• Nutrition and Vitamin	• Socio-economic status

Table 2: Symptoms of OA [17]

SYMPTOMS
Pain: The afflicted joints may experience pain during or after movement.
Stiffness: Joint stiffness may be more apparent in the morning or after inactivity.
Tenderness: When you lightly press on your joint, it could feel tenderness.
Diminution in adaptability: It might not be able to flex your joint all the way.
Grating feeling: When you utilize the joint, you could get a grating sensation and hear popping or cracking.
Bone growths. Around the afflicted joint, these additional pieces of bone that feel like hard lumps, can develop.
Swelling: Inflammation of the soft tissues near the joint may be the cause of this.

There are different sorts of management for knee osteoarthritis: non-surgical and surgical. When non-surgical modalities are no longer effective, the initial course of treatment switches to surgical intervention. Patient education, activity modification, physical therapy, weight loss, knee bracing, nonsteroidal anti-inflammatory medicines (NSAIDs), COX-2 inhibitors, glucosamine and chondroitin sulphate, corticosteroid injections, and hyaluronic acid are examples of non-surgical treatment options. Osteotomy, total knee arthroplasty (TKA) and unilateral knee arthroplasty are surgical options [15, 18]. Aceclofenac is compared with Etoricoxib in this study and when we look in to mechanism of action, both are similar in nature. Aceclofenac is a non-steroidal medication with pronounced analgesic and anti-inflammatory effects. Aceclofenac's mode of action is mostly dependent on the suppression of prostaglandin production. Aceclofenac significantly inhibits the enzyme cyclo-oxygenase, which is important for the production of prostaglandins. Aceclofenac's most frequent adverse effects are nausea, vomiting, diarrhea, flatulence, constipation, dyspepsia, Stomach discomfort, melaena, hematemesis, ulcerative stomatitis, aggravation of colitis, and aggravation of Crohn's disease [19]. A COX-2-selective inhibitor is etoricoxib (approximately 106 times more selective for COX-2 inhibition over COX-1). Etoricoxib specifically inhibits isoform 2 of the cyclo-oxygenase enzyme (COX-2) like any other COX-2 selective inhibitor, reducing the formation of prostaglandins (PGs) from arachidonic acid [20]. The following are a few common and significant side effects of etoricoxib: flu, indigestion, stomach ache, diarrhea, peripheral swelling, flatulence, weakness, fatigue [21].

Patients with OA often experience discomfort, restrictions on daily living activities, and a general decline in quality of life (QOL) as clinical consequences. Instruments for assessing QOL are needed in order to assess the severity of this burden, choose treatment modalities, and gauge their efficacy. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Medical Outcomes Study 36-Item Short-Form Health Survey are the 2 most often used tools to assess QOL and effectiveness of treatment in OA. Both offer helpful overall data about pain and function in OA patients to clinicians and researchers, although the WOMAC is more frequently utilized in clinical settings due to its self-administered nature. Other pain and function-specific measures are also available, and when combined with measures of overall QOL, they may offer more information about the patient's condition [22].

36-Item Short-Form Health Survey

The RAND 36-Item Health Survey covers the following eight health-related concepts: physical functioning, physiological pain, role constraints resulting from physical or emotional health difficulties, emotional well-being, social functioning, energy/fatigue, and general perceptions of health. A single item that shows a perception of a change in health is also included [23].

WOMAC

The Western Ontario and McMaster Universities Arthritis Index is used to assess hip and knee osteoarthritis (WOMAC). This self-administered questionnaire contains 24 items that are divided into 3 subscales: Pain (5 items): whether walking, climbing stairs, lying in bed, sitting, or standing [24].

MMAS-4

The MMAS consists of four items with a scoring system of "Yes" = 0 and "No" = 1. Medication

adherence primarily refers upon whether patients continue to take a prescribed medication as well as whether they take their prescriptions as directed (for example, twice daily). It is a generic self-reported medication-taking behavior scale where the "health concern" field is filled in with the relevant medical issue (high blood pressure, diabetes, elevated cholesterol, HIV, contraception, etc.). A range of scores from 0 to 4 are generated by adding the items [25].

OA is incurable, its prevalence is increasing and it is one of the leading causes of disability worldwide. With the growth of this OA population range, there is a need to encourage interventions to improve their quality of life and mental health [26]. Non-steroidal anti-inflammatory drugs (NSAID) are the first choice of treatment, since they reduce pain, improve functional ability. So, by comparing the effectiveness & safety of NSAID drugs (Etoricoxib & Aceclofenac used in the treatment of OA can enhance the quality of life.

MATERIALS AND METHODS

Study Design: This is a community based Cross-sectional study (prospective).

Study Duration:

Planning: 1 month
Data Collection: 3 months
Data Interpretation: 1 month
Thesis: Writing: 1 month

Study Centre: The study was conducted at selected orthopaedic clinics in T. Dasarahalli, Bengaluru District.

Sample Size: A total of 83 subjects were collected out of which 68 patients were selected for the study.

Inclusion Criteria:

- Patient diagnosed with osteoarthritis
- Patients above 18 years of age.
- Patients prescribed with Etoricoxib or Aceclofenac.

Exclusion Criteria:

- Those who are not willing to participate
- Patients prescribed with other analgesics.
- Other Rheumatologic/ Muscular disorder.

Source of Data:

The different sources of data were:

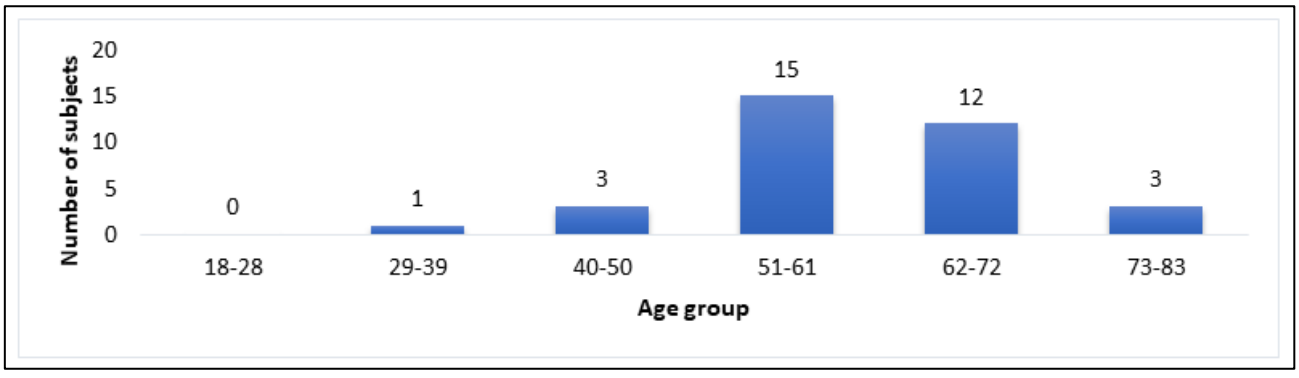
1. One to one interview with study subject.
2. Questionnaire

RESULTS

This study was conducted in selected Orthopaedics clinics in T. Dasarahalli, Bengaluru District. It was carried out for a period of 6 months, and 68 samples were collected. Among the 68 samples included, 34 samples were on Aceclofenac and the other 34 samples were on Etoricoxib.

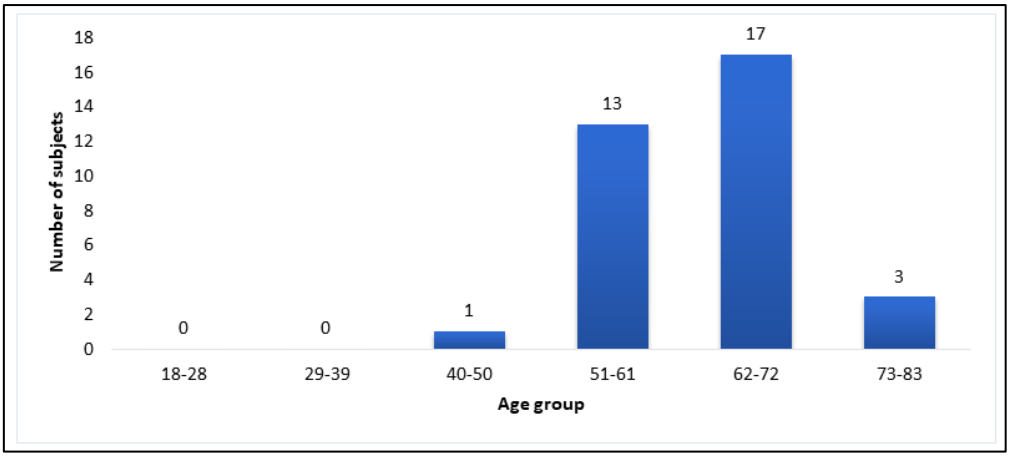
AGE DISTRIBUTION OF SUBJECTS IN ACECLOFENAC GROUP

The mean age of the study population was found to be 60.47 ± 9.44 years. Age group 51-61 years were in majority accounting for 44.12% of the total population and age group 29-39 were minimal in number i.e., 2.94% as shown in figure.



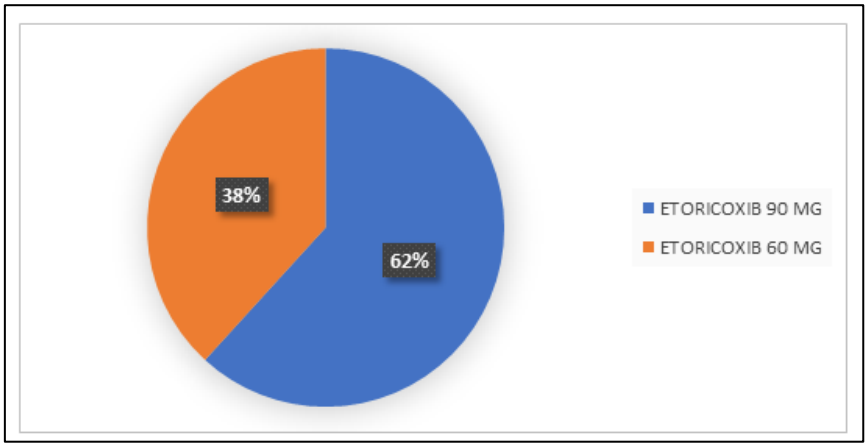
AGE DISTRIBUTION OF SUBJECTS IN ETOXICOXIB GROUP

The mean age of the study population was found to be 62.20 ±7.09 years. Age group 62-72 years were in majority accounting for 50% of the total population and age group 40-50 were minimal in i.e., 2.94% as shown in figure.



DOSE DISTRIBUTION AMONG SUBJECTS IN ETORICOXIB GROUP

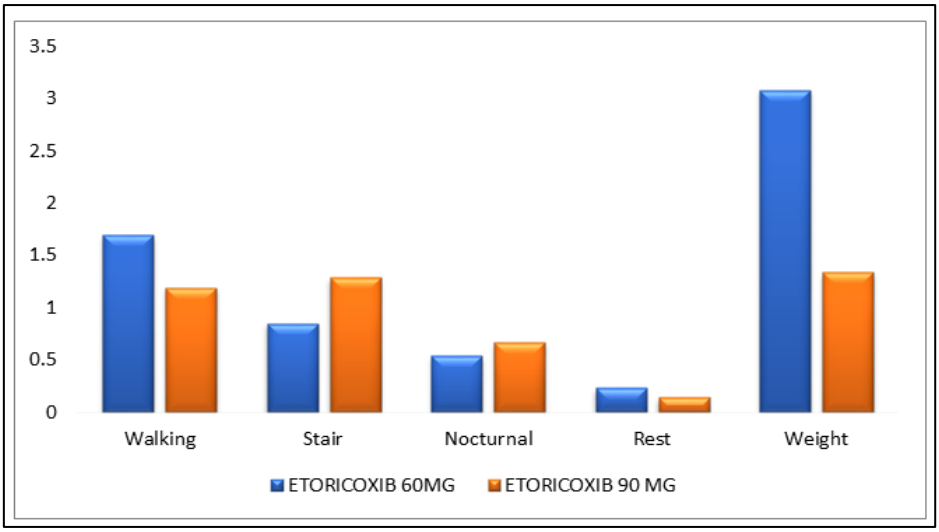
Out of 34 samples, 13 of them were taking Etoricoxib 60mg (38.24%) and 21 of them were taking Etoricoxib 90mg (61.76%) twice daily as shown in figure.

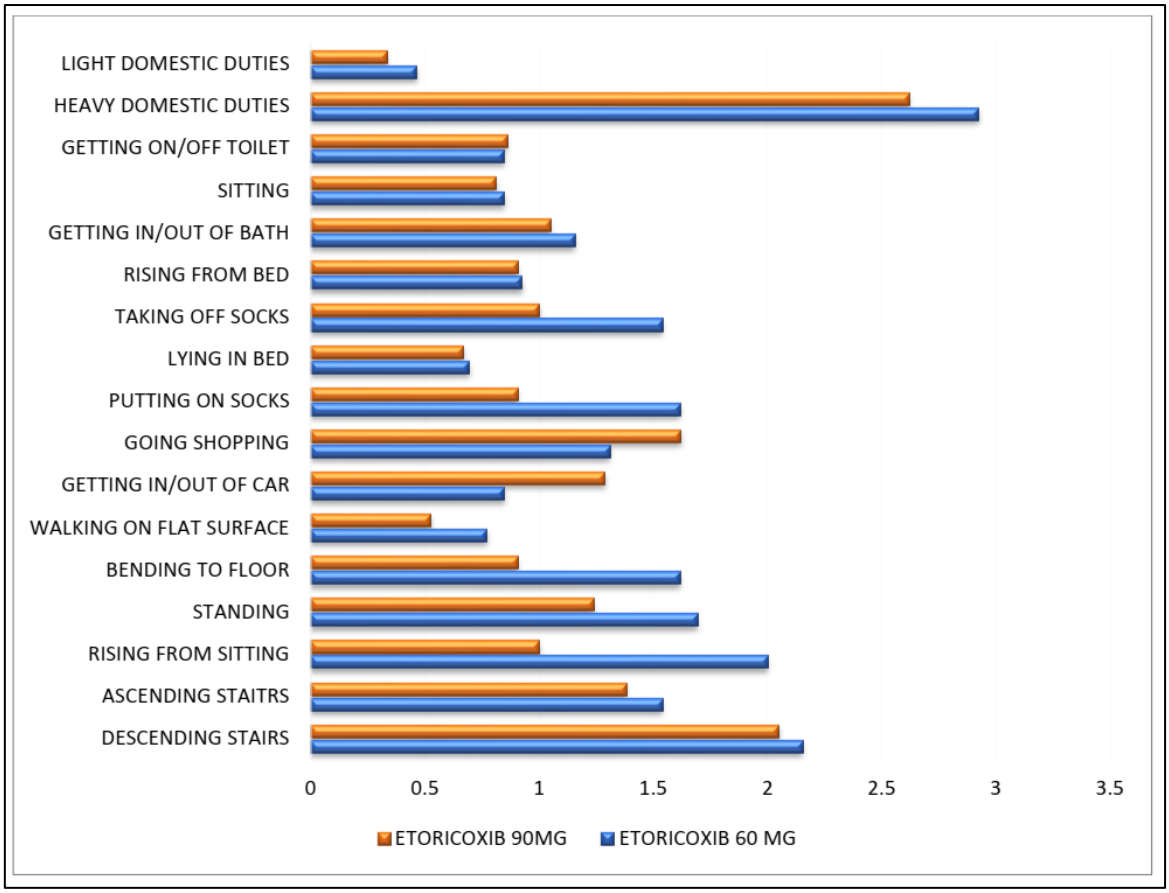


ASSESSMENT OF SAFETY AND EFFECTIVENESS IN ACECLOFENAC AND ETORICOXIB GROUP

Assessment of effectiveness in Etoricoxib subjects:

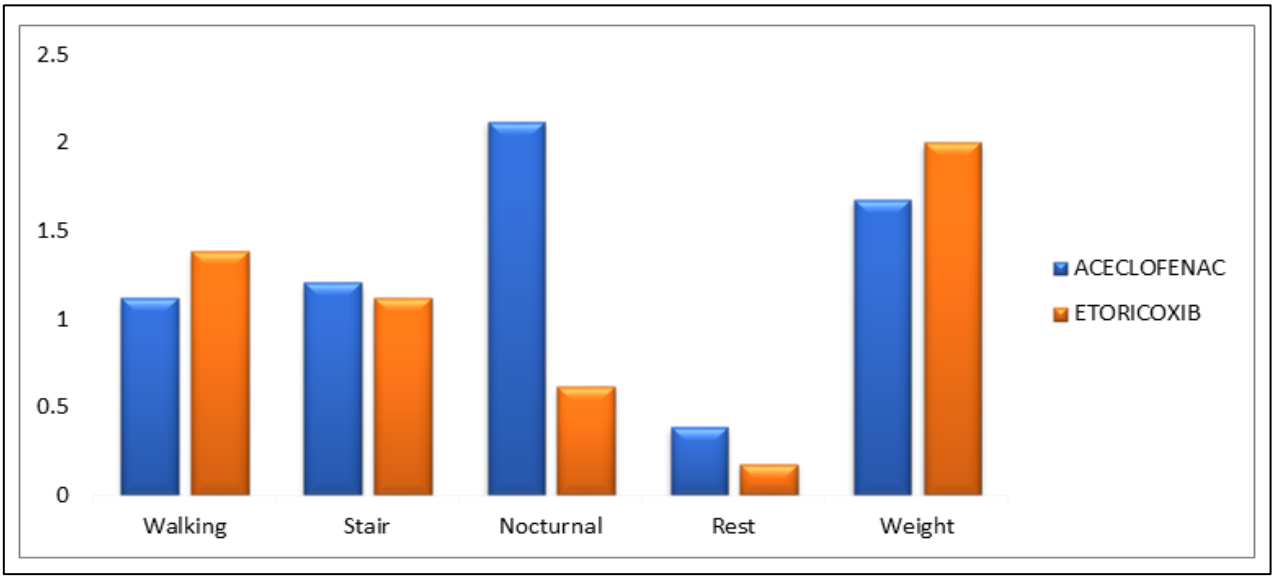
Etoricoxib 60mg was administered by 38.24% and 90mg was administered by 61.76% of the total population. By assessing the WOMAC Pain Scale in both groups, Etoricoxib 90mg was found to be more effective compared to the other.

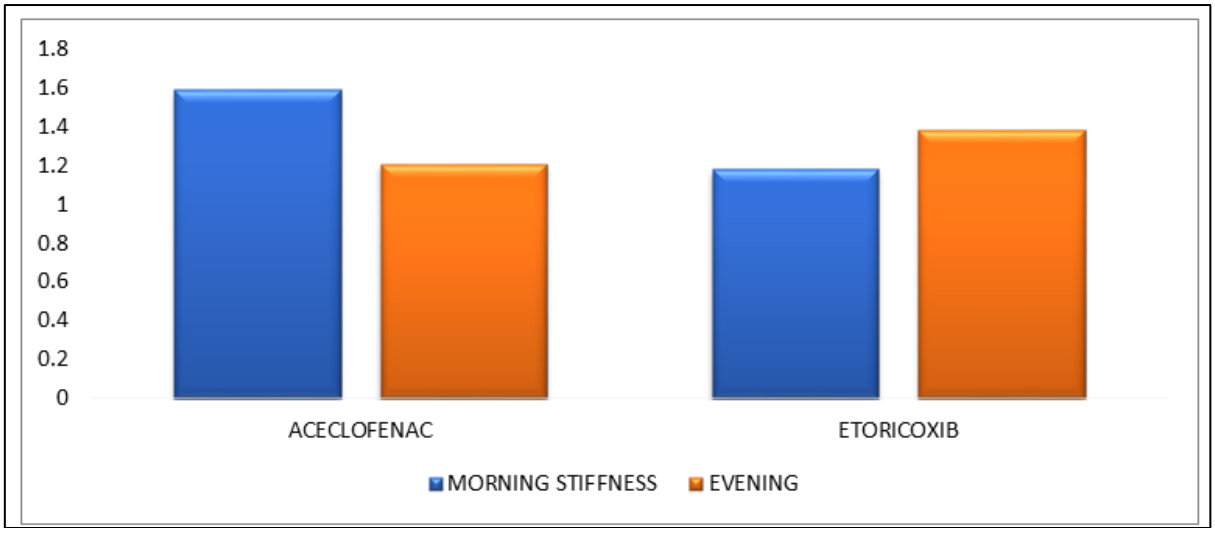


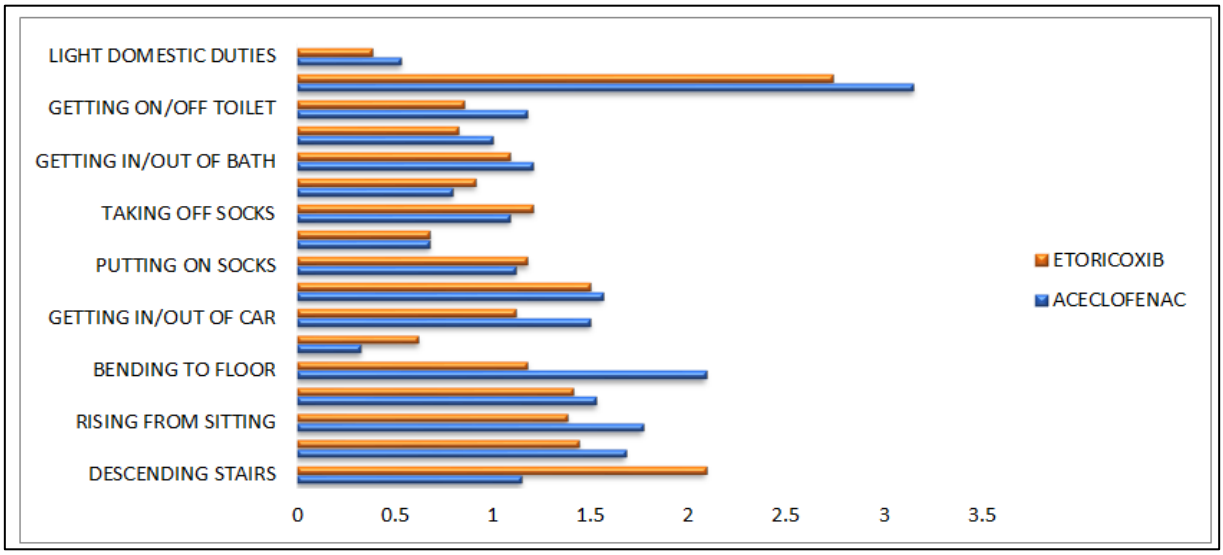


Comparison of effectiveness between Aceclofenac and Etoricoxib group:

A total of 68 samples were included in this study and the number of subjects were equally distributed in both groups as 34 samples (50%) in Aceclofenac and 34 samples (50%) in Etoricoxib group. On comparing the effectiveness of these drugs, both drugs were found to be effective in reducing pain.

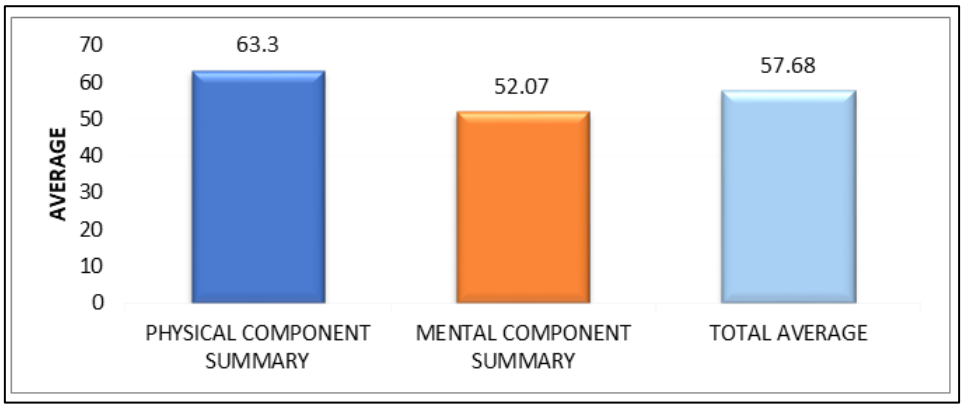






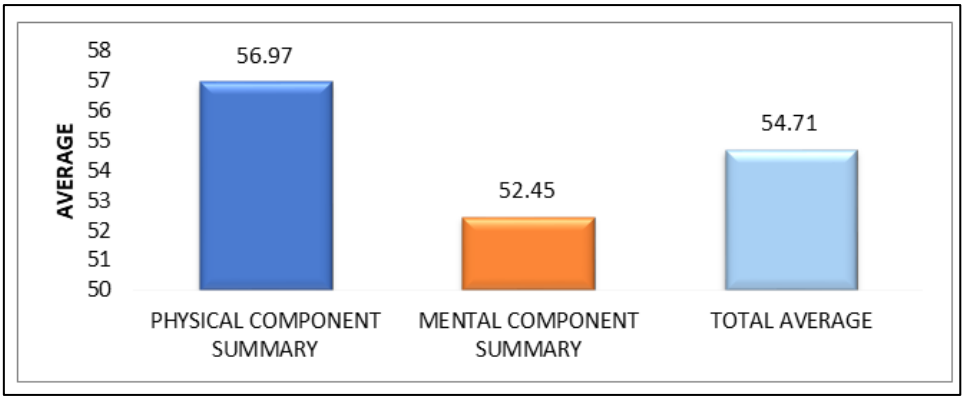
Average of PCS and MCS in Aceclofenac group:

The total average of four domains each under PCS and MCS was found to be 41.825 and 62.775 respectively. The overall average of both PCS and MCS was 52.3 as shown in figure.



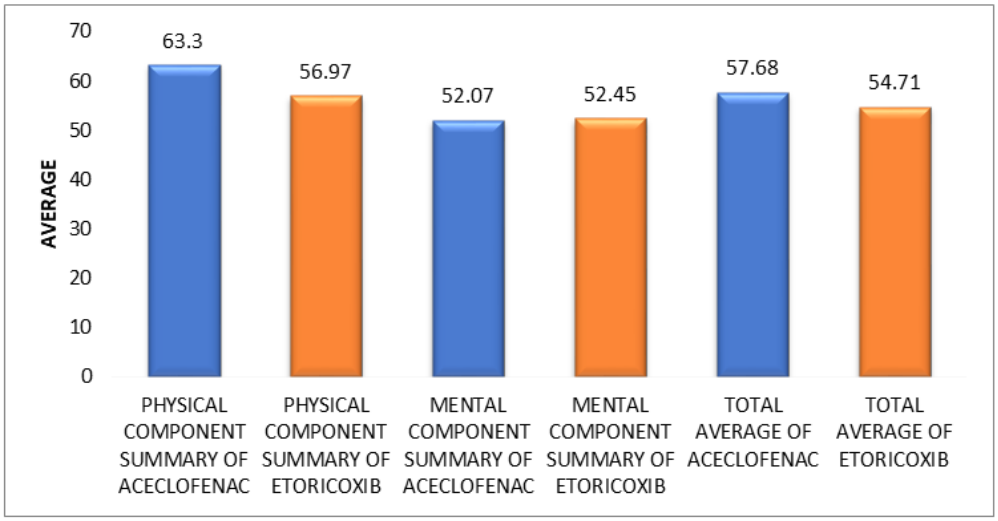
Average of PCS and MCS in Etoricoxib group:

The total average of four domains each under PCS and MCS was found to be 42.825 and 61.385 respectively. The overall average of both PCS and MCS was 52.105 as shown in figure.



Overall comparison of HRQL in Aceclofenac and Etoricoxib group:

On comparing the QOL scores in both Aceclofenac and Etoricoxib group, it was found that the subjects belonging to the Aceclofenac group had the highest overall mean score i.e., 57.68 when compared to overall mean score of Etoricoxib group i.e., 54.71.



DISCUSSION

This observational study was conducted in the selected Orthopaedic clinics in T. Dasarahalli, Bengaluru District for a period of 6 months by enrolling 68 subjects, based on various inclusion and exclusion criteria. The subjects were categorized according to age and gender. Out of the 68 subjects who participated in the study, majority of them belonged to the age group of 51-72 years (83.82%) (n=57) which is contrary to mean age of participants as in the study of Pareek A *et al*., [42]. The number of females (64.71%) (n=44) were more than the males (35.29%) (n=24) which is similar to the gender of participants designated as in the study of Curtis S *et al*., [43]. The study groups were categorized into two based on the drug they are taking, Aceclofenac group (n=34) and Etoricoxib group (n=34). The Etoricoxib group were classified again into two according to their doses Etoricoxib 60 mg (38.24%) (n=13) and 90 mg (61.76%) (n=21) which is alike to the study conducted by Chalini S *et al*., [44]. The present study compared treatment with Aceclofenac and Etoricoxib with regard to their safety and efficacy. On comparing the effectiveness of these drugs, both drugs were found to be effective in reducing pain in terms of efficacy parameters of WOMAC scores and investigator's assessment. Even if Etoricoxib was found to be superior than Aceclofenac in terms of reliving pain which is similar to the research conducted by Jung SY *et al*., [31]. Regarding the safety, Etoricoxib was found to be safer than Aceclofenac on assessing the side effects which is alike to the research conducted by Waraich HS *et al*., [32]. In our study Aceclofenac was showing more gastrointestinal side effects while Etoricoxib only produces minimal gastrointestinal side effects like constipation and mouth ulcer although the study had limitation in the time period and study samples owing to restriction in finding the exact safety of drugs. The HRQOL was assessed using SF-36 questionnaire. According to the results of the study the average scores for physical functioning, role limitation due to physical health, pain and general health of both Aceclofenac and Etoricoxib group was 67.6±24.4, 65.4±36.93, 66.91±23.12, 53.23±14.96 and 58.24±27.63, 64.71±35.42, 58.31±23.47, 46.62±15.94 respectively. While mean values of mental components including social functioning, role limitation due to emotional problems, energy and emotional wellbeing was found to

be 51.1±27.92, 65.6±38.03, 49.8±13.28, 41.8±11.23 and 56.74±26.28, 58.82±38.54, 48.38±14.96, 45.88±11.37, in Aceclofenac and Etoricoxib group respectively. On taking overall average of quality of life it was found to be little less in Etoricoxib than Aceclofenac group although Etoricoxib helps in improving quality of life of patients which is similar to the study done by Huang WN *et al*., [36] Analysis using Morisky Medication-Taking Adherence Scale-MMAS (4-item) revealed that out of 68 subjects 1 have high adherence, 29 have intermediate adherence and 38 have low adherence. Increasing adherence is one of the most crucial elements in the treatment of arthritic disorders. When a combination medicine is administered, medium adherence can be shown, and patients with low adherence require extra care. A patient would require a flawless score on the MMAS questionnaire in order to be considered for high adherence. For pain and other comorbid illnesses, many patients with OA are likely to be prescribed a variety of drugs; nevertheless, an increase in concurrent medications has been connected to a decline in medication adherence, the present study is comparable with study done by Conaghan PG *et al*., [45] in UK.

CONCLUSION

Osteoarthritis (OA), a long-term degenerative disease characterized by cartilage loss, is a complex illness, it greatly contributes to impairment and is extremely prevalent in society. In terms of WOMAC score efficacy metrics, Aceclofenac and Etoricoxib were found to be equally effective at reducing pain although Etoricoxib is slightly superior to Aceclofenac, in addition on comparing Etoricoxib 60 mg and 90 mg, 60mg was prominent and effective. Etoricoxib was determined to be safer than Aceclofenac when examining the side effects. Etoricoxib was shown to have a slightly lower overall average quality of life than the group receiving Aceclofenac. When it comes to physical condition, the Etoricoxib administering group outperforms the Aceclofenac consuming group, whereas Etoricoxib group is superior in terms of mental condition. One of the 68 participants in the analysis had a high level of adherence, 29 had intermediate adherence, and 38 had low adherence, according to the Morisky Medication-Taking Adherence Scale-MMAS (4-item). In a nutshell, the study accomplishes that better adherence should be provided in case of Osteoarthritis patients for improving their quality of life. Both these drugs were found to be equally effective in case of osteoarthritis management. Because of its enhanced safety profile, Etoricoxib is a better option than Aceclofenac for treating osteoarthritis symptoms.

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