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To assess and compare clinically and radiologically via T2 mapping the efficacy of a drug containing a combination of Rosehip extract, Boswellia serrata extract and Devil's claw extract with that of Diacerein in osteoarthritis knee

Dr. Gautam Sinha, Dr. Sanjay Sharma, Dr. Hardas Singh Sandhu
(Dept. of Orthopedics, Dr. Hardas Singh Orthopaedic Hospital & Super-speciality Research Centre, Amritsar, Punjab, India)

Abstract:
Background*: Osteoarthritis, the most prevalent form of arthritis is a chronic disorder of synovial joints in which there is progressive softening and disintegration of articular cartilage accompanied by new growth of cartilage and bone at the joint margins (osteophytes), cyst formation and sclerosis in the subchondral bone, mild synovitis and capsular fibrosis. It is associated with increased risk of mobility disability for those with affected knees being greater than that due to any other medical condition in people aged 65 years. Analgesics and anti-inflammatory drugs are the most common agents used in the management of knee osteoarthritis but these only act as symptomatic treatment and do not provide a cure and are associated with serious adverse events on gastrointestinal, renal and cardiovascular systems. The ideal treatment should modify the natural history of osteoarthritis and alter the articular cartilage destructive process. In the recent times, nutraceuticals are commonly used in the management of osteoarthritis knee in India and abroad. Since there are no studies comparing the different nutraceuticals on the basis of articular cartilage regeneration and clinical efficacy, we have selected this study to evaluate the efficacy of the four commonly used nutraceuticals for management of osteoarthritis in India, to evaluate their role and efficacy clinically and radiologically via T2 mapping,*
Materials and Methods*: In this comparative prospective single blinded study, 60 patients, both male and female belonging to age >30 years with signs (clinical and X-ray) and symptoms of osteoarthritis of one or both knee/knees were randomly allocated into 2 groups of 30 patients each, Group A (Drug I) and Group B (Drug II). Group A received Drug I which is an oral tablet containing a combination of Rosehip extract 275mg, Boswellia serrata extract 307.5mg and Devil's claw extract 100mg and group B received Drug II which is an oral tablet containing Diacerein 50mg. Both the drugs were administered for a period of 90 days. Assessment and comparison of the efficacy of the two drugs was done clinically via WOMAC score and radiologically via T2 mapping.*
Results*: The difference in the mean cartilage thickness pre-treatment and post-treatment of both the groups was not statistically significant. There was a statistically significant ($p<0.001$) decrease in the pre-treatment and post-treatment WOMAC score values of both groups. Patients in group-A had more decrease in the post treatment WOMAC score as compared to group-B.*
Conclusion: *The oral drug containing a combination of Rosehip extract, Boswellia serrata extract and Devil's claw extract is more effective in relieving symptoms of osteoarthritis knee when compared to oral Diacerein.*
Key Word*: **Osteoarthritis knee; Rosehip extract; Boswellia serrata extract; Devil's claw extract; Diacerein; WOMAC; T2 mapping.***

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I. Introduction

Osteoarthritis is a chronic disorder of synovial joints in which there is progressive softening and disintegration of articular cartilage accompanied by new growth of cartilage and bone at the joint margins (osteophytes), cyst formation and sclerosis in the subchondral bone, mild synovitis and capsular fibrosis. In its most common form, it is unaccompanied by any systemic illness and, although there are sometimes local signs of inflammation, it is not primarily an inflammatory disorder. Cartilage softening and disintegration are accompanied from the very outset by hyperactive new bone formation, osteophytosis and remodelling. The final picture is determined by the relative vigor of these opposing processes[(1)]. Osteoarthritis is a multifactorial process in which mechanical factors have a central role and is characterized by changes in structure and function of the whole joint[(2)]. Osteoarthritis is the most prevalent form of arthritis, with an associated risk of mobility disability (defined as needing help walking or climbing stairs) for those with affected knees being greater than

that due to any other medical condition in people aged 65 years[3]. Almost, 45% of women over the age of 65 years are suffering from osteoarthritis of knee[4,5]. It affects more than 80% of people over the age of 55 years and the prevalence increases with age[6,7]. The recent high incidence of osteoarthritis is observed in younger age group also[8]. Among 20-year-olds, the prevalence of osteoarthritis is 9%, increasing to 30% in individuals >60 years, and 90% in those between 70 and 74 years of age[9].The prevalence in India is found to be 28.7%[10]. Osteoarthritis in weight-bearing joints is strongly linked to body mass index. Obesity and overweight is a significant risk factor[11]. Obese individuals have 1.5 to 2 times greater risk of developing knee osteoarthritis as compared to their leaner counterparts[12]. More commonly, there is preferential narrowing of the medial tibiofemoral compartment accompanied by narrowing of the patellofemoral compartment[13].

Plain radiographs have been used primarily in the evaluation of osteoarthritis, which depict only narrowing of the joint space or gross osseous changes that tend to occur late in the disease. Early changes in the articular cartilage may not be visible on plain radiographs. Cartilage loss can only be indirectly inferred by the development of joint space narrowing, which can be highly unreliable even with careful attention to proper technique. In addition, plain radiographs do not reveal focal cartilage loss, and widening of the joint space despite significant cartilage loss can occur in one compartment of the knee simply as a result of narrowing in the outer compartment. Standard cartilage dedicated MR techniques, are also inconclusive in quantifying early degenerative changes of the cartilage matrix, especially biochemical changes in cartilage.

MRI based T2 mapping method allows for the indirect assessment of collagen content and orientation, which are important indicators for early osteoaarthritis. The collagen matrix of healthy cartilage traps and immobilizes water protons, so signal intensity on T2-weighted images is low. In the earliest stages of osteoaarthritis, the matrix begins to break down and becomes more permeable to water, causing an elevation in T2 relaxation times. T2 mapping has been shown to be able to detect changes in the water content, collagen structure, and orientation and organization of cartilage, all of which are associated cartilage degradation[14,15,16]. For in vivo imaging of the knee joint, an increase in T2 was associated with aging [17,18] and the involvement of osteoarthritis[14].

Analgesics and anti-inflammatory drugs are the most common agents used in the management of knee osteoarthritis[19]. These only act as symptomatic treatment and do not provide a cure of osteoarthritis[20] and are associated with serious adverse events on gastrointestinal, renal and cardiovascular systems. The ideal treatment should modify the natural history of osteoarthritis and alter the articular cartilage destructive process. Such substances which protect the articular cartilage during osteoarthritis are termed as 'chondroprotective agents,'[21].

In the recent times, Nutraceuticals are used commonly in the management of osteoarthritis knee in India and abroad. The term "nutraceuticals" was coined from 'nutrition' and 'pharmaceuticals' in 1989 by DeFelicen[22] and was described as food that provides medical or health benefits.

In the current study, we have investigated the role of four commonly used nutraceuticals in the management of knee osteoarthritis in India, to evaluate their role and efficacy clinically and radiologically via T2 Mapping. First drug is a combination of rosehip extract, boswellia serrata extract and devil's claw extract and the second drug is diacerein. The purpose of the study is therefore to assess knees, clinically and radiologically via T2 Mapping in varying stages of osteoarthritis for improvement in clinical symptoms and regeneration of articular cartilage respectively after a period of 90 days of treatment.

II. Material And Methods

This prospective comparative single blinded type of study was carried out on patients at Dr. Hardas Singh Orthopaedic Hospital and Super-speciality Research Centre, Amritsar, Punjab, India from October 2017 to September 2019. A total of 60 adult subjects (both male and females) of aged >30 years were used for in this study.

Study Design: Comparative prospective single blinded type of study.
Study Location: This was a tertiary care teaching hospital based study done at Dr. Hardas Singh Orthopaedic Hospital and Super-speciality Research Centre, Amritsar, Punjab, India.

Study Duration: October 2017 to September 2019.
Sample size: 60 patients.
Subjects & selection method: The study population was drawn from patients suffering from osteoarthritis knee who presented at Dr. Hardas Singh Orthopaedic Hospital & Super-speciality Research Centre and had undergone clinical examination and radiological examination via T2 mapping of the affected knee/knees before treatment initiation between from October 2017 to September 2019. Patients were randomly divided into two groups (each group had 30 patients). The prescribed doses of the two drugs are as follows:

Group A (N = 30 patients) – Drug I containing Rosehip extract 275mg, Boswellia serrata extract 307.5mg and Devil's claw extract 100mg daily to each patient for 90days.
Group B (N = 30 patients) – Drug II containing Diacerein 50mg daily to each patient for 90days.

Inclusion criteria:
1. Age >30 years
2. Either sex
3. Admitted and/or seen on out-patient basis with signs (clinical and X-ray) and symptoms of osteoarthritis of the knee.
4. Patients willing to participate in the study.

Exclusion criteria:
1. Patients not willing to participate in the study.
2. Patients with history of surgery or intra-articular steroid injection.
3. Patients with history of neuropathic joints or infection.
4. Patients suffering from joint pathologies other than osteoarthritis (psoriatic arthritis, gouty arthritis, systemic lupus erythematosus, bone tuberculosis) or, having other serious systemic disorders.
5. Pregnant and lactating women.
6. Patients with substantial abnormalities in the hematological, hepatic, renal or metabolic functions.
7. Patients who received glucosamine sulfate, chondroitin sulfate, intra-articular hyaluronate, or systemic or intra-articular glucocorticoids in the 6 weeks preceding enrolment in the study.

Procedure methodology:

After explaining the procedure in detail a written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients. The questionnaire included socio-demographic characteristics such as age, sex, height, weight, body mass index (BMI), affected knee and duration of the pain.

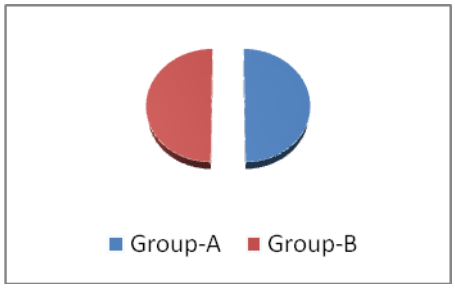
Baseline Clinical examination and T2 mapping of the affected knee/knees were done. The Western Ontario and McMaster University (WOMAC) osteoarthritis index was used to determine the function, quality of life, and joint pain. All subjects completed the WOMAC questionnaire for the affected knee/knees on the day clinical examination and MR T2 map images were acquired both pre-treatment and post-treatment. Assessment of the joint function and any regeneration of the articular cartilage were performed based on the changes in the WOMAC score and MR T2 mapping respectively after 90 days of oral course of the drugs being administered.

Statistical analysis:

The data from the present study was systematically collected, compiled and statistically analyzed to draw relevant conclusions. Sample size was calculated keeping in view at most 5% risk with minimum 85% power and 5% significance level (significant at 95% confidence interval). Data was analyzed by using paired 't' test. The p-value was determined finally to evaluate the levels of significance. The p-value of >0.05 was considered non-significant; p-value of 0.01 to 0.05 was considered significant and p-value of <0.001 was considered highly significant. The results were then analyzed and compared to previous studies. SPSS-22 version of software was used, released 2013, Armonk, NY: IBM Corp.

III. Results

Total number of patients in our study were 60. Out of which 30 (50%) were in group-A and 30 (50%) were in group-B.



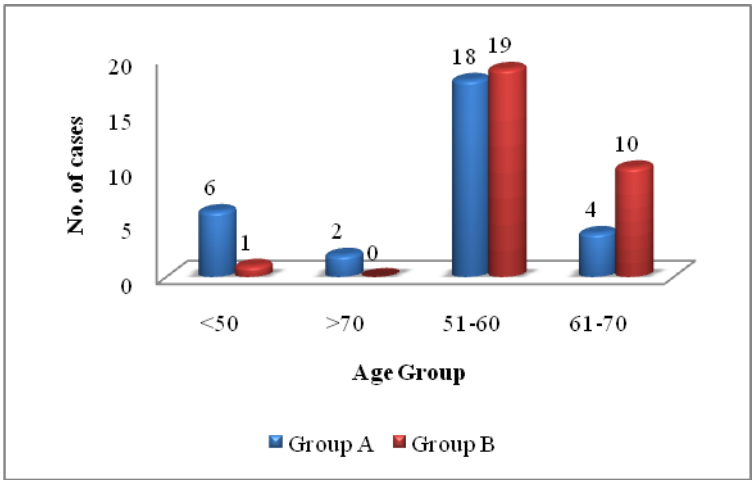
Graph 1: Pie chart showing distribution of number of patients between the two study groups.

Age Distribution:
60 cases of OA knee above the age of 30 years were included in the present study.

In this study 7 (11.67%) of the total patients were less than 50 years of age, 2 (3.33%) more than 70 years, 37 (61.67%) between 51-60 years and 14 (23.33%) were between 61-70 years of age.
In Group-A**,** 6 (20%) patients were less than 50 years of age, 2 (6.67%) patients were more than 70 years, 18 (60%) were between 51-60 years, 4 (13.33%) were between 61-70 years of age. The mean age of the patients in this group was 57.17±7.00 years.
In Group-B, 1 (3.33%) patient was less than 50 years of age, 19 (63.33%) between 51-60 and 10 (33.33%) were between 61-70 years of age. The mean age of the patients in this group was 59.10±4.32 years.

Table 4: Age distribution in the two study groups and in total.

Age group (in years)	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
<50	6	20.00	1	3.33	7	11.67
>70	2	6.67	0	0.00	2	3.33
51-60	18	60.00	19	63.33	37	61.67
61-70	4	13.33	10	33.33	14	23.33
Total	30	100.00	30	100.00	60	100.00
Mean age	57.17±7.00		59.10±4.32			



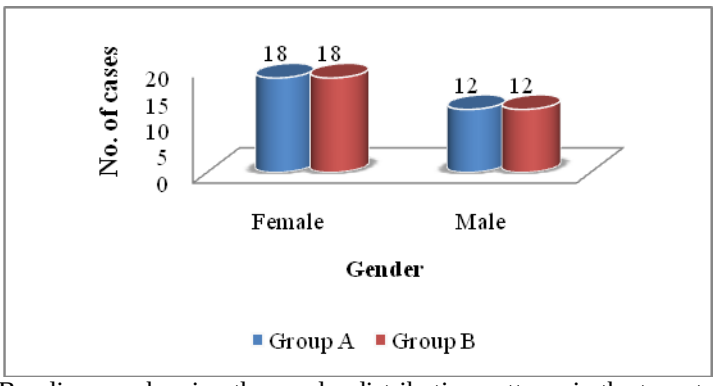
Graph 2: Bar diagram showing the age distribution in the two study groups.

Gender Distribution:

Overall, the two groups combined there were more number of females, n=36 (60%) as compared to males, n=24 (40%) in this study. But there were equal number of females, n=18 (60%) and males, n=12 (40%) in both the individual study groups.

Table 5: Gender distribution in the two study groups and in total.

Gender	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
Female	18	60.00	18	60.00	36	60.00
Male	12	40.00	12	40.00	24	40.00
Total	30	100.00	30	100.00	60	100.00



Graph 3: Bar diagram showing the gender distribution patterns in the two study groups.

Height Distribution:

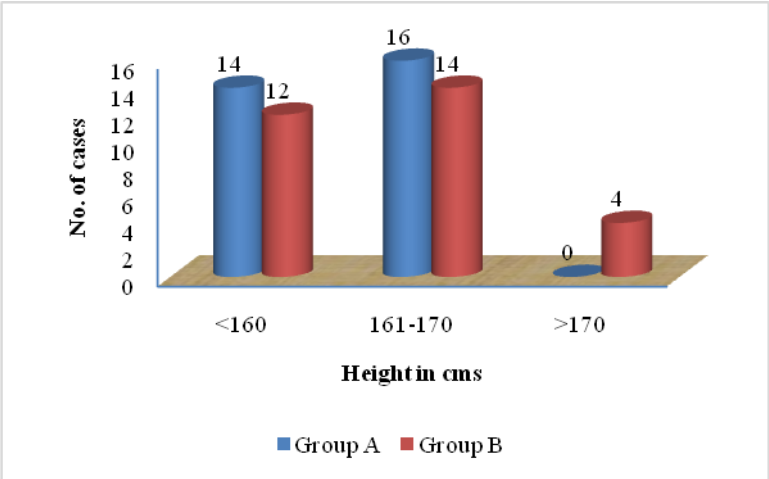
In this study 26 (43.33%) of the total patients were less than 160 cm in height, 30 (50%) between 161-170 cm and 4 (6.67%) were more than 170 cm in height.

In Group-A, 14 (46.67%) patients were less than 160 cm in height and 16 (53.33%) between 161-170 cm. Mean height of the patients in this group was 160.93±5.99 cm.

In Group-B, 12 (40%) patients were less than 160 cm in height, 14 (46.67%) between 161-170 cm and 4 (13.33%) were more than 170 cm in height. Mean height of the patients were 161.20±6.85 cm.

Table 6: Height distribution in the two study groups and in total.

Height (in cms)	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
<160	14	46.67	12	40.00	26	43.33
161-170	16	53.33	14	46.67	30	50.00
>170	0	0.00	4	13.33	4	6.67
Total	30	100.00	30	100.00	60	100.00
Mean height	160.93 ± 5.99		161.20 ± 6.85			



Graph 4: Bar graph showing the height distribution in the two study groups.

Weight Distribution:

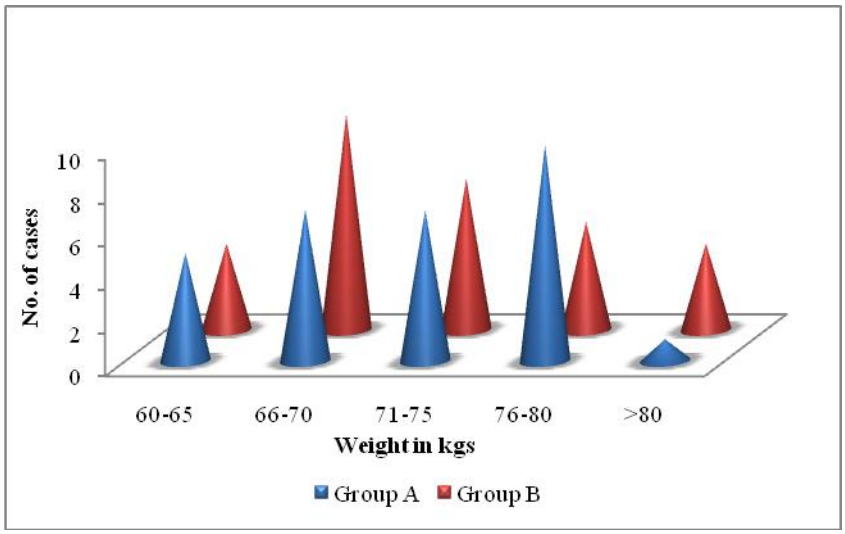
In this study 9 (15%) of the total patients were between 60-65 kg in weight, 17 (28.33%) between 66-70 kg, 14 (23.33%) between 71-75 kg, 15 (25%) between 76-80 kg and 5 (8.33%) were more than 80 kg.

In Group-A, 5 (16.67%) of the patients were between 60-65 kg in weight, 7 (23.33%) between 66-70 kg, 7 (23.33%) between 71-75 kg, 10 (33.33 %) between 76-80 kg and 1 (3.33%) was more than 80 kg. Mean weight of the patients were 72.28±5.70 kg.

In Group-B, 4 (13.33%) of the patients were between 60-65 kg in weight, 10 (33.33%) between 66-70 kg, 7 (23.33%) between 71-75 kg, 5 (16.67 %) between 76-80 kg and 4 (13.33%) were more than 80 kg. Mean weight of the patients were 72.201±7.04 kg.

Table 7: Weight distribution in the two study groups and in total.

Weight (in kgs)	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
60-65	5	16.67	4	13.33	9	15.00
66-70	7	23.33	10	33.33	17	28.33
71-75	7	23.33	7	23.33	14	23.33
76-80	10	33.33	5	16.67	15	25.00
>80	1	3.33	4	13.33	5	8.33
Total	30	100.00	30	100.00	60	100.00
Mean weight	72.28±5.70		72.01±7.04			



Graph 5: Graph showing the weight distribution in the two study groups.

BMI Distribution:

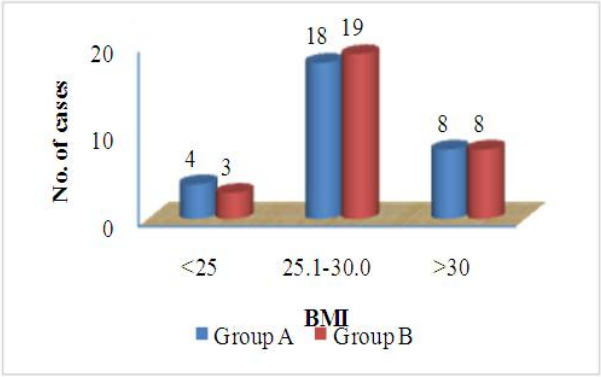
In this study, BMI of 7 (11.67 %) of the total patients werebetween 18.5-24.9 kg/m^2, 37 (61.67%) between 25.0-29.9 kg/m^2 and 16 (26.67%) were more than 30 kg/m^2.

In Group-A, BMI of 4 (13.33 %) patients were between 18.5-24.9 kg/m^2, 18 (60%) between 25.0-29.9 kg/m^2 and 8 (26.67 %) were more than 30 kg/m^2. Mean BMI in this group was 28.07±2.90 kg/m^2.

In Group-B, BMI of 3 (10 %) patients were between 18.5-24.9 kg/m^2, 19 (63.33 %) between 25.0-29.9 kg/m^2 and 8 (26.67%) were more than 30 kg/m^2. Mean BMI in this group was 27.73±2.64 kg/m^2.

Table 8: BMI distribution in the two study groups and in total.

BMI (in kg/m$^{2)}$	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
18.5-24.9	4	13.33	3	10.00	7	11.67
25.0-29.9	18	60.00	19	63.33	37	61.67
>30	8	26.67	8	26.67	16	26.67
Total	30	100.00	30	100.00	60	100.00
Mean BMI	28.07±2.90		27.73±2.64			



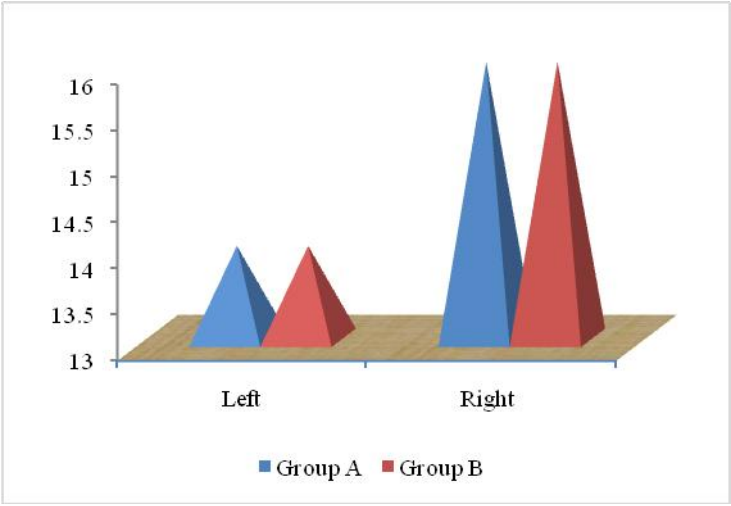
Graph 6: Bar graph showing the BMI distribution in the two study groups

Side Distribution:

In this study, both groups had equal distribution of knee sides involved. Right knee, n=16 (53.33%) was involved more than the left knee, n=14 (46.67%) in both the groups.

Table 9: Side distribution in the two study groups and in total.

Side involved	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
Left	14	46.67	14	46.67	28	46.67
Right	16	53.33	16	53.33	32	53.33
Total	30	100.00	30	100.00	60	100.00



Graph 7: Bar graph showing the distribution of involved side in the two study groups.

Kellgren-Lawrence Grade Distribution:

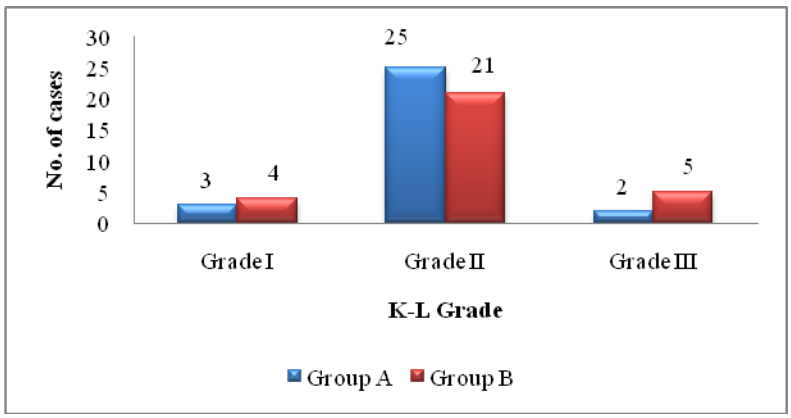
In this study we found that most of the patients in both the groups belong to K-L Grade II.

In Group-A, 3 (10%) of the patients were K-L Grade-I, 25 (83.33%) were Grade-II and 2 (6.67%) were Grade-III.

In Group-B, 4 (13.33%) of the patients were K-L Grade-I, 21 (70%) were Grade-II and 5 (16.67%) were Grade-III.

Table 10: K-L grade distribution in the two study groups and in total.

K-L Grade	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
Grade- I	3	10.00	4	13.33	7	11.67
Grade-II	25	83.33	21	70.00	46	76.67
Grade-III	2	6.67	5	16.67	7	11.67
Total	30	100.00	30	100.00	60	100.00



Graph 8: Bar graph showing the K-L grade distribution in the two study groups

WOMAC SCORE DISTRIBUTION:

WOMAC score for Group-A:

The mean pre-treatment pain sub-score was 10.60±2.80 and the mean post-treatment pain sub- score was 6.83±2.82.

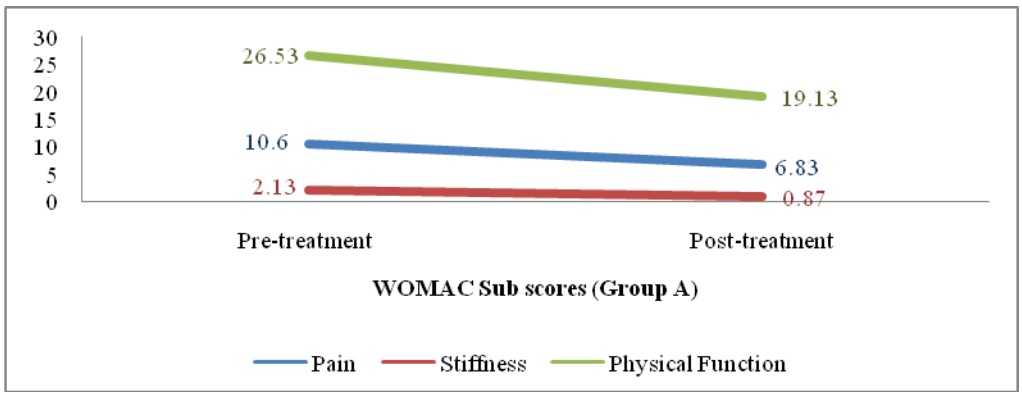
The mean pre-treatment stiffness sub-score was 2.13±1.11 and the mean post-treatment stiffness sub-score was 0.87±0.78.

The mean pre-treatment physical function sub-score was 26.53±8.54 and the mean post-treatment physical function sub-score was 19.13±8.33.

The total mean pre-treatment WOMAC sub-score was 39.07±10.73 and the total mean post-treatment WOMAC sub-score was 27.50±10.66.

Table 11a: WOMAC score distribution of group-A, Pre-treatment and Post-treatment.

WOMAC score	Pre-treatment		Post treatment		p-value
	Mean	SD	Mean	SD	
Pain	10.60	2.80	6.83	2.82	<0.001
Stiffness	2.13	1.11	0.87	0.78	<0.001
Physical Function	26.53	8.54	19.13	8.33	<0.001
Total	39.07	10.73	27.50	10.66	<0.001



Graph 9a: Line diagram showing the WOMAC sub group scores distribution pre-treatment and post treatment in group-A,

WOMAC score for Group-B:

The mean pre-treatment pain sub-score was 9.37±3.82 and the mean post-treatment pain sub-score was 6.80±2.85.

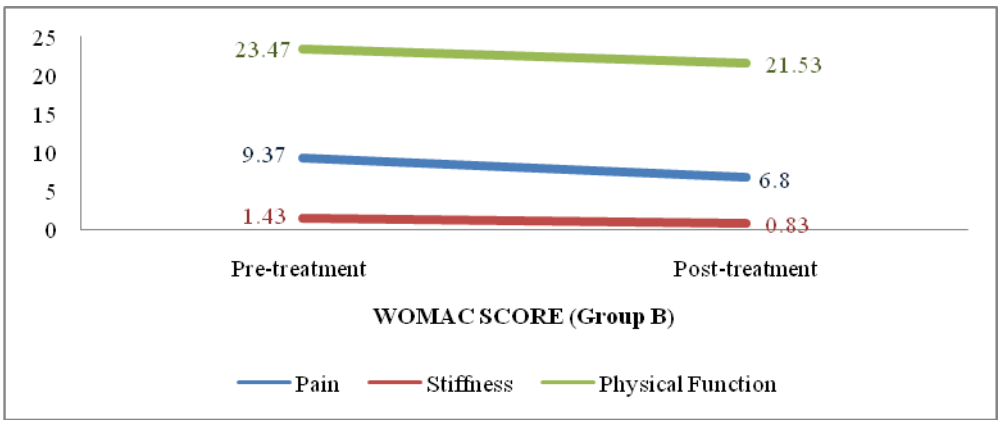
The mean pre-treatment stiffness sub-score was 1.43±1.43 and the mean post-treatment stiffness sub-score was 0.83±1.12

The mean pre-treatment physical function sub-score was 23.47±6.62 and the mean post-treatment physical function sub-score was 21.53±6.54.

The total mean pre-treatment WOMAC sub-score was 34.27±8.47 and the total mean post-treatment WOMAC sub-score was 28.27±8.13.

Table 11b: WOMAC score distribution of group-B, Pre-treatment and Post-treatment.

WOMAC score	Pre-treatment		Post treatment		p-value
	Mean	SD	Mean	SD	
Pain	9.37	3.82	6.80	2.85	<0.001
Stiffness	1.43	1.43	0.83	1.12	<0.001
Physical Function	23.47	6.62	21.53	6.54	<0.001
Total	34.27	8.47	28.27	8.13	<0.001



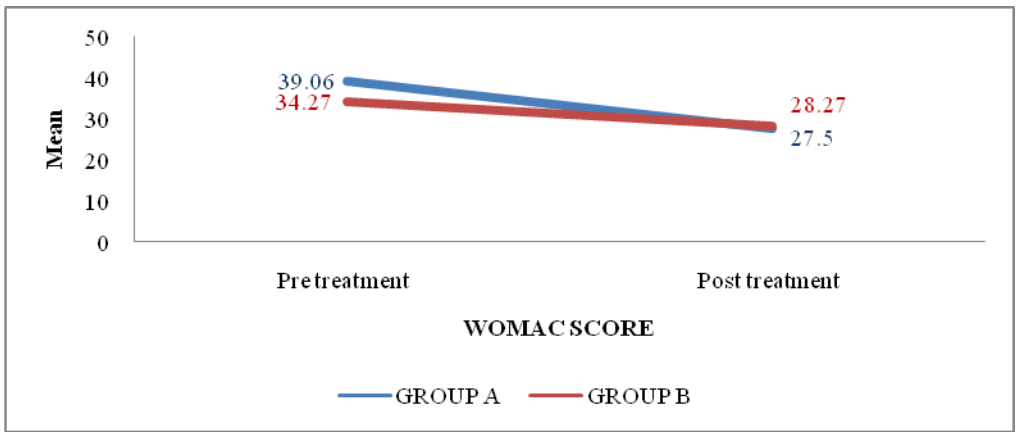
Graph 9b: Line diagram showing the WOMAC sub group scores distribution pre-treatment and post treatment in group-B.

The mean total pre-treatment and post-treatment WOMAC score of Group-A were 39.07±10.73 and 27.50±10.66 respectively.

The mean total pre-treatment and post-treatment WOMAC score of Group-B were 34.27±8.47 and 28.27±8.13 respectively.

Table 11c: Mean total WOMAC score distribution of group-A and group-B, Pre-treatment and Post-treatment.

Group	WOMAC score pre treatment		WOMAC score post treatment		p-value
	Mean	SD	Mean	SD	
Group A	39.07	10.73	27.50	10.66	<0.001
Group B	34.27	8.47	28.27	8.13	<0.001



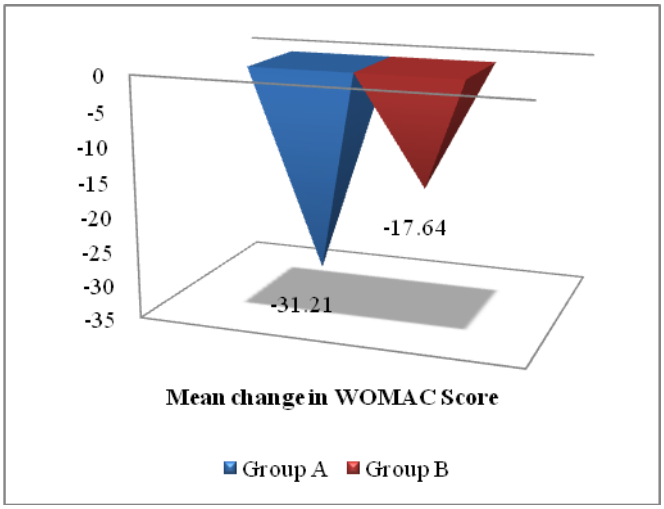
Graph 9c: Line diagram showing the total mean WOMAC score distribution pre-treatment and post treatment in group-A and group-B.

In this study we found that both the total and individual post-treatment WOMAC sub-scores decreased highly significantly as compared to the pre-treatment values for both the groups, Group-A (p<0.001) and group-B (p<0.001) respectively.

Also the mean decrease in the total post-treatment WOMAC of group-A was 31.21±11.28% and that of group-B was 17.64±11.32% which is highly significant (p<0.001) for both groups, although patients in group-A had more decrease in the post treatment WOMAC score as compared to post treatment WOMAC score of patients in group-B.

Table 11d: Mean difference in WOMAC score distribution of group-A and group-B compared to pre-treatment values.

Group	Mean change in WOMAC score	SD	p-value
Group-A	-31.21	11.28	<0.001
Group-B	-17.64	11.32	<0.001



Graph 10: Showing the mean change in WOMAC score in the two study groups from the pre-treatment values.

T2 MAP GRADE DISTRIBUTION:

Out of the total 60 patients, there were more patients with grade-II 41(68.33%) T2 map grade followed by grade-I 13 (21.67%) and grade-III 6 (10%).

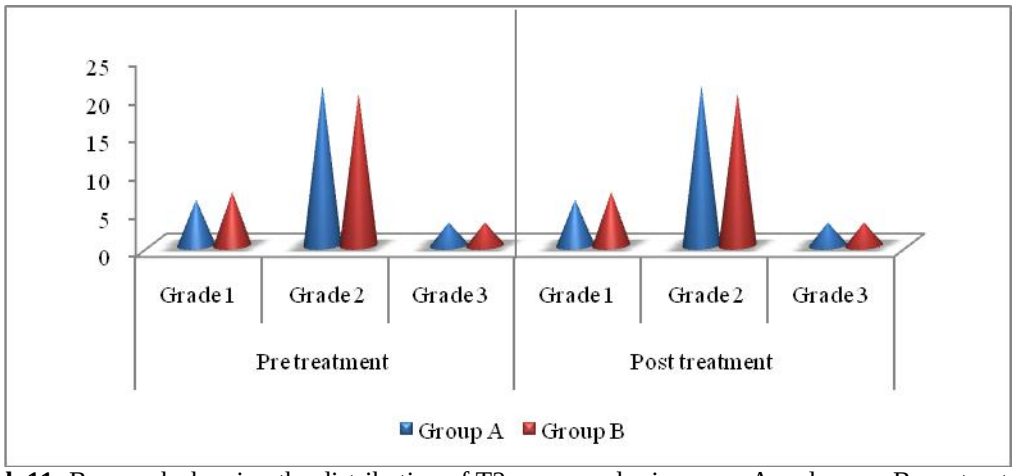
In Group-A, there were 6 (20%) patients with grade-1 T2 mapping grade, 21 (70%) with grade-2 and 3 (10%) with grade-3.

In Group-B, there were 7 (23.33%) patients with grade-1 T2 mapping grade, 20 (66.67%) with grade-2 and 3 (10%) with grade-3.

We found no difference in the pre-treatment and post-treatment T2 map grading values of both group-A and group-B.

Table 12: Distribution of T2 map grades in the two groups and in total pre-treatment and post-treatment.

T2 Map grade	Group-A		Group-B		Total	
Pre-Treatment	No.	%	No.	%	No.	%
Grade-1	6	20.00	7	23.33	13	21.67
Grade-2	21	70.00	20	66.67	41	68.33
Grade-3	3	10.00	3	10.00	6	10.00
Post-Treatment	Group-A		Group-B		Total	
Grade-1	6	20.00	7	23.33	13	21.67
Grade-2	21	70.00	20	66.67	41	68.33
Grade-3	3	10.00	3	10.00	6	10.00



Graph 11: Bar graph showing the distribution of T2 maps grades in group-A and group-B pre-treatment and post- treatment.

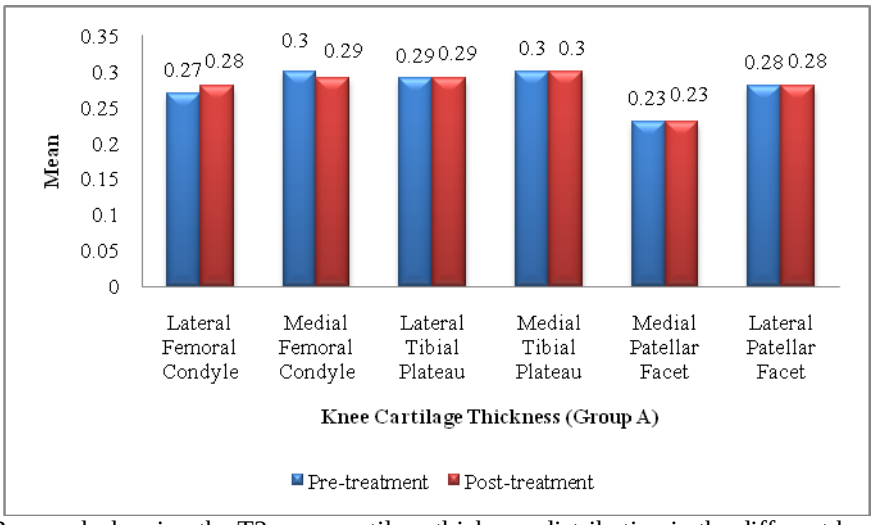
CARTILAGE THICKNESS DISTRIBUTION:

For group-A, mean pre-treatment values of lateral femoral condyle is 0.27±0.05 cm, medial femoral condyle is 0.30±0.06 cm, lateral tibial plateau is 0.29±0.09 cm, medial tibial plateau 0.30±0.09 cm, medial patellar facet 0.23±0.08 cm and lateral patellar facet is 0.28±0.09 cm.

For group-A, mean post-treatment values of lateral femoral condyle is 0.28±0.05 cm, medial femoral condyle is 0.29±0.07 cm, lateral tibial plateau is 0.29±0.08 cm, medial tibial plateau 0.30±0.10 cm, medial patellar facet 0.23±0.08 cm and lateral patellar facet is 0.28±0.09 cm.

Table 13a: Showing the T2 map thickness distribution in the different cartilages in Group-A pre-treatment and post- treatment.

Knee cartilage thickness (Group-A)	Pre-treatment		Post-treatment		p-value
	Mean	SD	Mean	SD	
Lateral Femoral Condyle	0.27	0.05	0.28	0.05	0.012
Medial Femoral Condyle	0.30	0.06	0.29	0.07	0.004
Lateral Tibial Plateau	0.29	0.09	0.29	0.08	0.448
Medial Tibial Plateau	0.30	0.09	0.30	0.10	0.360
Medial Patellar Facet	0.23	0.08	0.23	0.08	0.484
Lateral Patellar Facet	0.28	0.09	0.28	0.09	0.506
Total Thickness	1.67	0.32	1.66	0.31	0.244



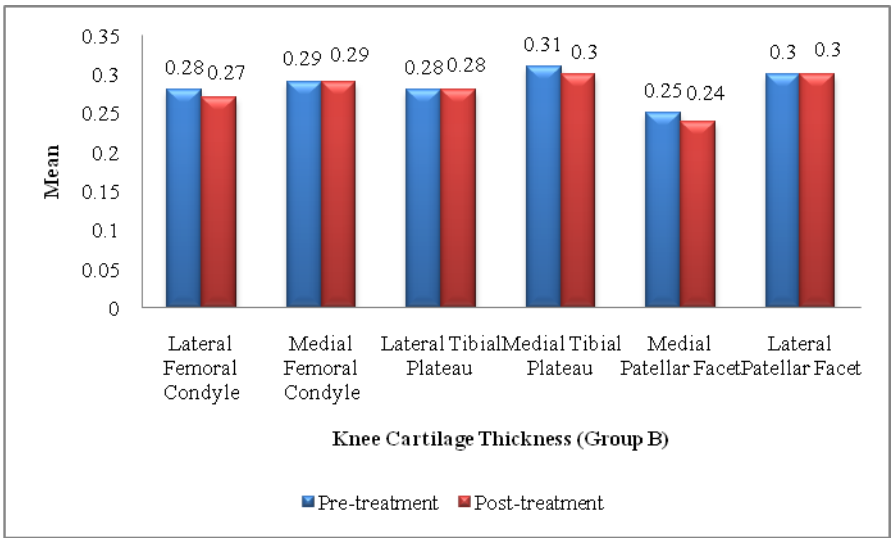
Graph 12a: Bar graph showing the T2 maps cartilage thickness distribution in the different knee cartilages in Group-A pre-treatment and post-treatment.

For group-B, mean pre-treatment values of lateral femoral condyle is 0.28±0.08 cm, medial femoral condyle is 0.29±0.06 cm, lateral tibial plateau is 0.28±0.08 cm, medial tibial plateau 0.31±0.07 cm, medial patellar facet 0.25±0.07 cm and lateral patellar facet is 0.30±0.07 cm.

For group-B, mean post-treatment values of lateral femoral condyle is 0.27±0.08 cm, medial femoral condyle is 0.29±0.06 cm, lateral tibial plateau is 0.28±0.08 cm, medial tibial plateau 0.30±0.07 cm, medial patellar facet 0.24±0.07 cm and lateral patellar facet is 0.30±0.07 cm.

Table 13b: Showing the cartilage thickness distribution in the different knee cartilages in Group-B pre-treatment and post-treatment.

Knee cartilage thickness (Group-B)	Pre-treatment		Post-treatment		p-value
	Mean	SD	Mean	SD	
Lateral Femoral Condyle	0.28	0.08	0.27	0.08	0.011
Medial Femoral Condyle	0.29	0.06	0.29	0.06	0.003
Lateral Tibial Plateau	0.28	0.08	0.28	0.08	0.030
Medial Tibial Plateau	0.31	0.07	0.30	0.07	0.037
Medial Patellar Facet	0.25	0.07	0.24	0.07	0.021
Lateral Patellar Facet	0.30	0.07	0.30	0.07	0.234
Total Thickness	1.71	0.25	1.69	0.25	0.121

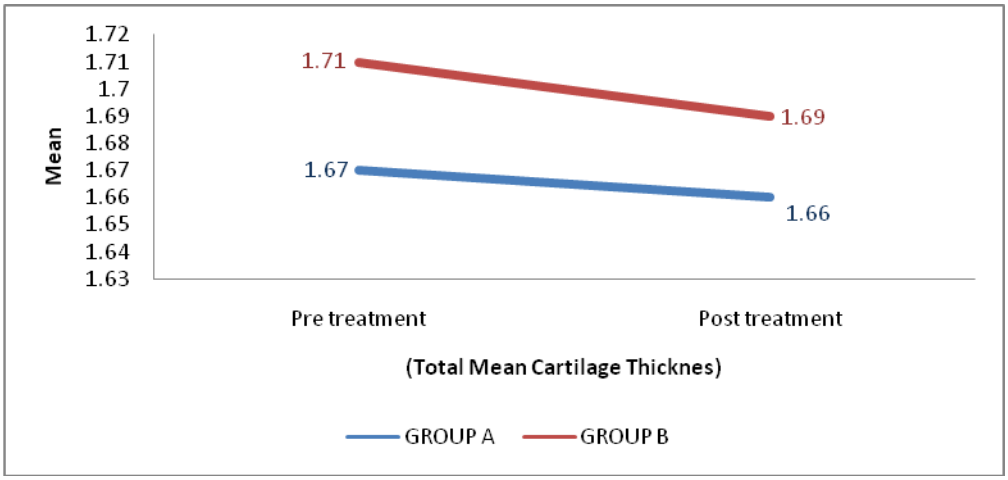


Graph 12b: Bar graph showing the T2 map cartilage thickness distribution in the different knee cartilages in Group- B pre-treatment and post-treatment.

The pre-treatment mean total thickness of cartilage in group-A is 1.67±0.32 and that of group-B is 1.71±0.25 cm.
The post-treatment mean total thickness of cartilage in group-A was 1.66±0.31 and that of group-B is 1.69±0.25 cm.
The difference in the pre-treatment and the post-treatment values of both groups were not significant (p-value of Group-A 0.244 and Group-B 0.121).

Table 13c: Showing the total mean T2 map cartilage thickness distribution in the different knee cartilages in Group- A and Group-B pre-treatment and post-treatment

Group	Total mean thickness pre-treatment		Total mean thickness post-treatment		p-value
	Mean	SD	Mean	SD	
Group-A	1.67	0.32	1.66	0.31	0.244
Group-B	1.71	0.25	1.69	0.25	0.121



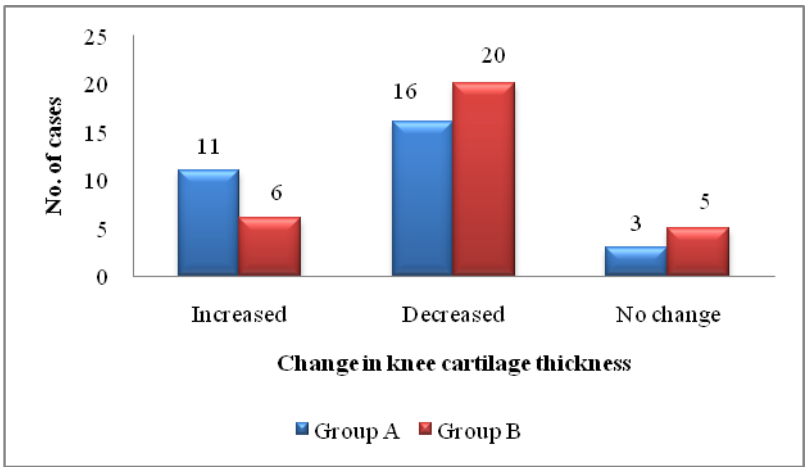
Graph 12c: Line diagram showing the total mean T2 map cartilage thickness distribution in the different knee cartilages in Group-A and Group-B pre-treatment and post-treatment.

In this study, in Group-A, 11 (36.66%) cases had increased cartilage thickness, 16 (53.33%) cases had decreased cartilage thickness and 3 (10%) cases had no change in the cartilage thickness compared to the pre-treatment values.

In Group-B, 6 (20%) cases had increased cartilage thickness, 20 (66.66%) had decreased cartilage thickness and 4 (13.33%) cases had no change in the cartilage thickness compared to the pre-treatment values.

Table 13d: Showing the change in knee cartilage thickness post-treatment in Group-A, Group-B and in total.

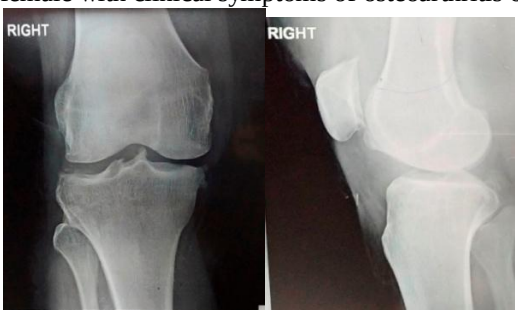
Change in Cartilage Thickness	Group-A		Group-B		Total	
	No.	%	No.	%	No.	%
Increased	11	36.66	6	20.01	17	28.33
Decreased	16	53.33	20	66.66	36	60.01
No change	3	10.01	4	13.33	7	11.66
Total	30	100	30	100	60	100



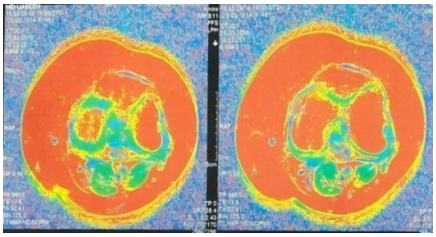
Graph 12d: Bar graph showing the change in knee cartilage thickness after treatment in the two study groups.

Case No. 6 (Group-A)

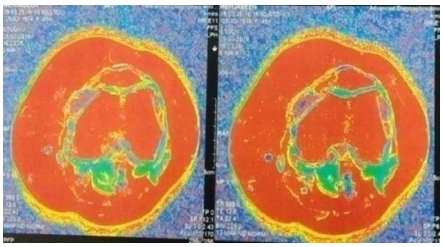
45 year old female with clinical symptoms of osteoarthritis of right knee



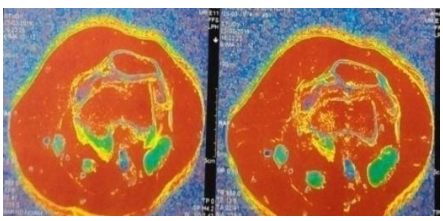
A. Left Knee – AP and Lateral views; K-L Grade II



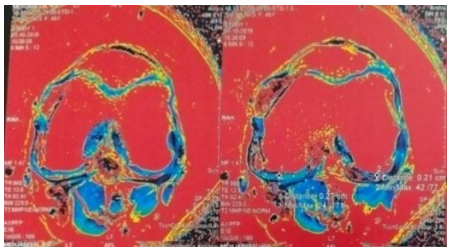
B. Pre-treatment T2 map: LFC=0.27cm, MFC=0.33cm



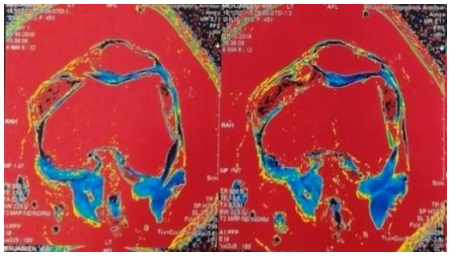
C. Pre-treatment T2 map: LTP=0.25cm, MTP=0.24cm



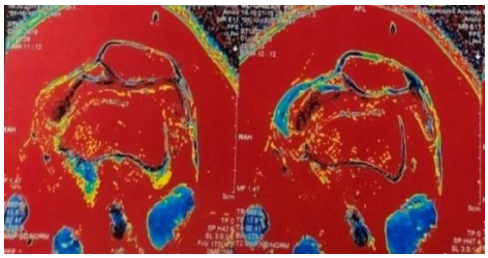
D. Pre-treatment T2 map: MPF=0.14cm, LPF=0.14cm



E. Post-treatment T2 map: LFC=0.30cm, MFC=0.28cm



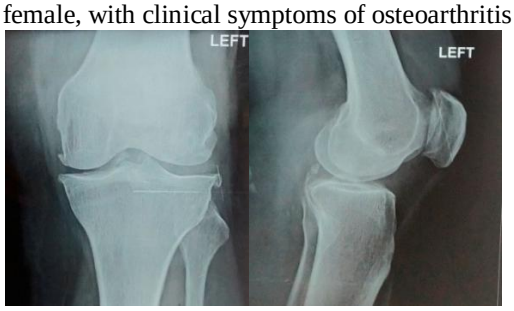
F. Post-treatment T2 map: LTP=0.29cm, MTP=0.18cm



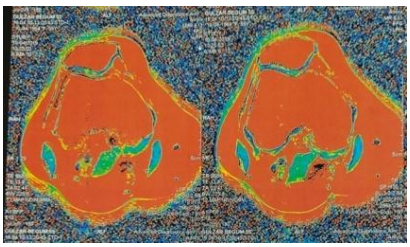
G. Post-treatment T2 map: MPF=0.17cm, LPF=0.17cm

Case No. 14 (Group-A)

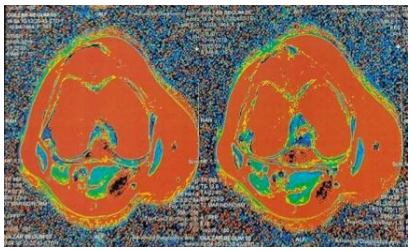
55 year old female, with clinical symptoms of osteoarthritis right knee.



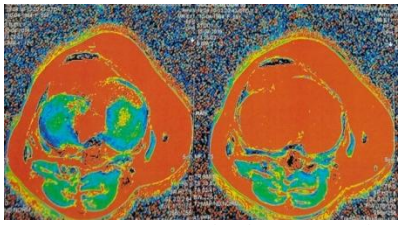
A. Left Knee – AP and Lateral views; K-L Grade II



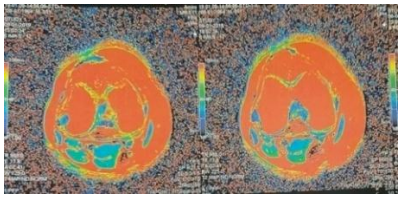
B. Pre-treatment T2 map: LFC=0.14cm, MFC=0.18cm



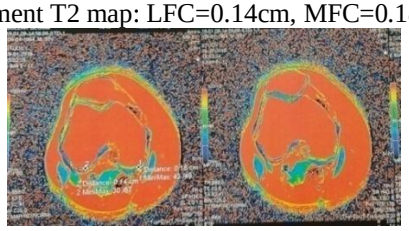
C. Pre-treatment T2 map:LTP=0.14cm, MTP=0.14cm



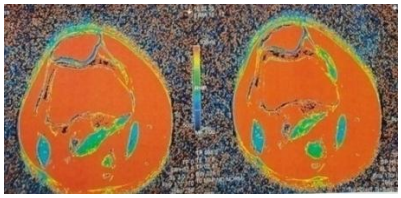
D. Pre-treatment T2 map:MPF=0.16cm, LPF=0.28cm



E. Post-treatment T2 map: LFC=0.14cm, MFC=0.18cm



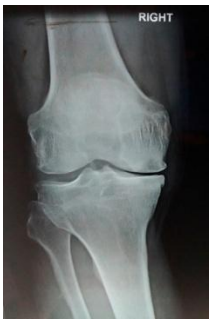
F. Post-treatment T2 map:LTP=0.15cm, MTP=0.14cm



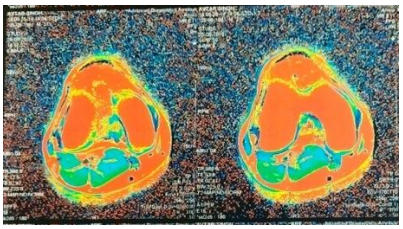
G. Post-treatment T2 map:MPF=0.16cm, LPF=0.29cm

Case No. 5 (Group-B)

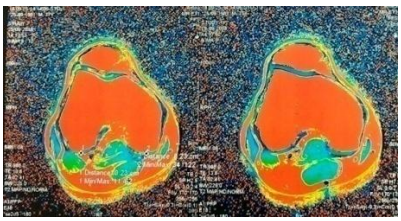
57 year old male, with clinical symptoms of osteoarthritis right knee.



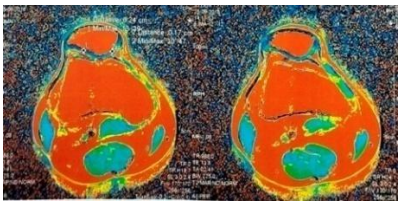
A. Left Knee – AP view; K-L Grade II



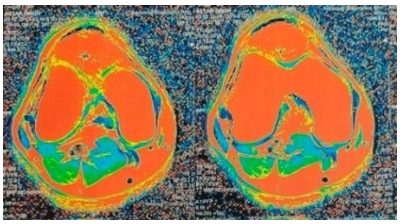
B. Pre-treatment T2 map: LFC=0.22cm, MFC=0.25cm



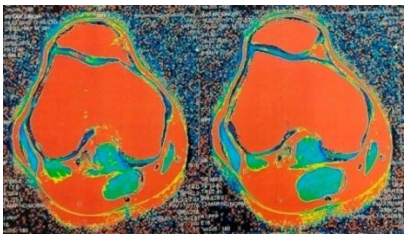
C. Pre-treatment T2 map:LTP=0.15cm, MTP=0.26cm



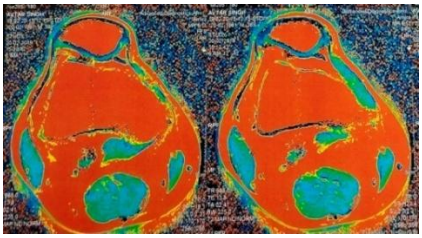
D. Pre-treatment T2 map:MPF=0.15cm, LPF=0.27cm



E. Post-treatment T2 map: LFC=0.22cm, MFC=0.26cm



F. Post-treatment T2 map:LTP=0.15cm, MTP=0.27cm



G. Post-treatment T2 map:MPF=0.17cm, LPF=0.29cm

IV. Discussion

Knee osteoarthritis is a multifactorial disease with a significant population burden[(23)]. Novel strategies in the management of knee osteoarthritis are based on early detection and minimally invasive procedures[(24,25)]. Many in vivo studies have demonstrated an association between increased T2/T1ρ values and various stages of osteoarthritis about the knee[(26)].

One of the hallmark of osteoarthritis is progressive loss of hyaline cartilage, initiated by a loss of proteoglycans and an increase in water content, followed by loss of type-II collagen and a change in collagen fiber orientation. Progression of osteoarthritis is usually graded based in plain radiographs, using joint space width, continuity of bony contours, and the presence and size of osteophytes as criteria[(27)]. However, these criteria do not help for the detection of early cartilage changes[(28)]. As articular cartilage has only limited capability for self-repair an early diagnosis of cartilage degeneration and a sensitive non-invasive diagnostic tool are highly desirable.

Recent MRI studies have included measurements of biomechanical and biochemical properties if cartilage such as GAG and water content as well as the collagen organization and content[(29)]. A technique reported to quantify cartilage water content and collagen fiber orientation is quantitative T2 mapping. Focal increase in T2 relaxation time has been associated with cartilage matrix damage, in particular a loss of collagen integrity and an increase in water content[(30)].

In this study, we found the body mass index (BMI) of most of the patients to be overweight (61.67%), followed by obese (26.67%) and normal BMI (11.67%). In group-A 60% of the patients were overweight and in group-B 61.67% of the patients were overweight. In group-A the mean BMI was 28.07±2.90 and in group-B, 27.73±2.64 which is a non-significant difference.

In a study by Apel at al[(31)] (2005) to determine whether a herbal remedy made from a subspecies of rose-hip extract might reduce symptoms of osteoarthritis and consumption of rescue medication in patients suffering from osteoarthritis, they had 94 patients (54 women and 40 men) in their study divided into two groups A and B found the mean BMI to be 27.3kg/m2 and 26.6 kg/m2 which is a non-significant difference.

In this study, there was a highly significant decrease in both the total and individual post-treatment WOMAC score and sub-score respectively in both the groups. There was a highly significant decrease in the post-treatment WOMAC score compared to pre-treatment values, but patients in group-A has more significant decrease in the WOMAC score compared to group-B.

Sontakke, S. et al[(32)] in 2006 in a randomized, prospective, open-label, comparative study in 66 patients in 6 months to compare the efficacy, safety and tolerability of boswellia serrata extract in osteoarthritis knee with valdecoxib, a selective COX-2 inhibitor found that the boswellia serrata extract group had significant difference in the WOMAC score versus baseline only after 2 months of therapy ($p<0.001$). At the end of 7 months, WOMAC score was significantly lower ($p<0.001$) than with valdecoxib for all three parameters.

Wegener, T. and Lüpke[(33)] in 2003 in a study on 75 patients to assess the efficacy of Devil's claw extract on arthrosis and low back pain found that there was a strong reduction of pain and the symptoms of osteoarthritis, and there was a relevant improvement of each WOMAC subscale as well as of the total WOMAC index.

Brahmachari B. et al[(34)] in 2009 in their study of 64 patients in a randomized single blinded placebo controlled study to evaluate the efficacy and safety of diacerein in early, symptomatic OA knee in Indian population found that compared to placebo diacerein showed significant reduction ($p<0.05$) in WOMAC physical function score.

In this study, most of the patients had Grade-2 T2 map grading followed by Grade-1 and Grade-3 in both Group-A and Group-B. We found no difference in the pre-treatment and post-treatment T2 map grades in both the study groups.

On comparing the thickness of knee cartilage for both the groups pre-treatment and post-treatment values, we found no statistically significant increase in the total post-treatment cartilage thickness. Rather, there was an overall decrease in the mean cartilage thickness for both group-A and group-B compared to the pre-treatment values but was not significant (p-value Group-A=0.244 and Group-B=0.121).

V. Conclusion

Our study has demonstrated the efficacy of two drugs, first is an oral combination of Rosehip extract, Boswelia serrata extract and Devil's claw extract and second is Diacerein in relieving pain and improving physical function in osteoarthritis knee but the drug containing the combination of Rosehip extract, Boswelia seratta extract and Devil's claw extract is more effective than Diacerein in relieving symptoms of osteoarthritis knee.

It also demonstrated that both the drugs have no role in increasing the cartilage thickness in osteoarthritis knee.

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