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A Comparative Study Of Functional Outcome After Intra Articular Injection Of Platelet Rich Plasma Alone Therapy Vs PRP+HA Combination Therapy In Grade-2 And Grade-3 Knee Osteoarthritis: A Prospective Study.

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Abstract:

Background

Osteoarthritis (OA) is a chronic, progressive degenerative joint disease primarily caused by wear and tear, affecting the articular cartilage, subchondral bone, ligaments, and synovium. Knee osteoarthritis (KOA), the most common form of OA, predominantly affects the elderly, significantly impairing daily activities and quality of life. Among non-surgical treatments, Platelet-Rich Plasma (PRP) and Hyaluronic Acid (HA) therapies have gained attention for their potential to alleviate symptoms. This study investigates the effectiveness of PRP therapy versus a combination of PRP and HA in managing pain, stiffness, and physical function in patients with mild to moderate KOA.

Materials &Methods

A Prospective Observational study was conducted for 6 months (Aug-2023 to feb-2024) in department of Obstetrics and Gynaecology in Sri Balaji Medical College, Hospital & research Institute (SBMCH&RI), Renigunta. A total of 50 patients, aged 50–65 years, diagnosed with Grade II or Grade III KOA were included in this randomized clinical trial. Participants were divided into two groups: 1. The PRP group received PRP therapy alone. 2. The PRP+HA group received a combination of PRP and HA therapy.

Both interventions were administered as injections into the affected knee. Outcomes were assessed using the Visual Analogue Scale (VAS) for pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain, stiffness, and physical function. Follow-up evaluations were conducted over a six-week period. Data were analyzed using the student's t-test to compare the effectiveness of the two therapies, with statistical significance set at $p < 0.05$.

Results

Both groups demonstrated improvements in VAS and WOMAC scores over the study period. However, the PRP+HA group exhibited significantly greater improvements compared to the PRP group: Pain reduction: More substantial in the PRP+HA group ($p < 0.05$). Stiffness improvement: PRP+HA group outperformed the PRP group ($p < 0.05$). Physical function: Significant enhancement in the PRP+HA group ($p < 0.05$).

Conclusion

We concluded that PRP+HA combination therapy (synergistic effects) can improve VAS & WOMAC scores (after 6 weeks of treatment) and enhanced benefits in alleviating symptoms and improving joint function function in patients with Grade II and Grade III KOA.

Keywords: *Osteoarthritis, knee osteoarthritis, Platelet rich plasma, Hyaluronic acid, Kellgren- Lawrence grading scale, VAS scale, WOMAC scale.*

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I. Introduction:

Knee osteoarthritis: Knee osteoarthritis (KOA), also known as chronic progressive degenerative joint disease of the knee, is typically the result of wear and tear and progressive loss of articular cartilage, subchondral bone, ligaments, capsule, and synovium. It is most common in the elderly.1

Epidemiology:

The burden of knee osteoarthritis extends far, being a leading cause of disability and carrying significant economic implications both within India and worldwide. Osteoarthritis is the second most prevalent rheumatologic issue and stands as the predominant joint ailment in India, with a prevalence ranging from 22% to 39%. OA is more common in women than men, but the prevalence increases dramatically with age. Nearly, 45% of women over the age of 65 years have symptoms while radiological evidence is found in 70% of those over 65 years. 2&3

Aetiology:

Osteoarthritis (OA) is classified into:

1. Primary OA (Idiopathic or Non-traumatic)

Occurs without a clear cause, associated with factors like:

Age, Obesity, Genetics, Occupation, Metabolic disorders.

2. Secondary OA (Traumatic or Mechanical Misalignment)

Trauma, Postsurgical changes, Rheumatoid arthritis, Infectious arthritis, Gout, Hyperparathyroidism, Haemophilia, Acromegaly, Hyperthyroidism, Malposition (varus/valgus), Wilson's Disease, Rickets, Avascular necrosis, Sickle cell disease, Psoriatic arthritis, Paget's Disease. 4

Risk factors of knee OA:

Modifiable: Overweight, Muscle weakness, Articular trauma, Occupation, Health-metabolic syndrome, Joint laxity, Kneeling, Squatting, Meniscal injuries

Non modifiable: Age, Gender and ethnicity (females more common than males), Genetics, Race 5&6

Mechanism / pathogenesis:

The primary pathological characteristics of KOA include degradation and degeneration of articular cartilage. Other manifestations include articular cartilage softening, fibrosis, ulceration, and the loss of articular cartilage, synovial hyperaemia, swelling and hyperplasia, subchondral bone sclerosis and eburnation and osteophyte formation and subchondral cyst formation. 7,8&9.

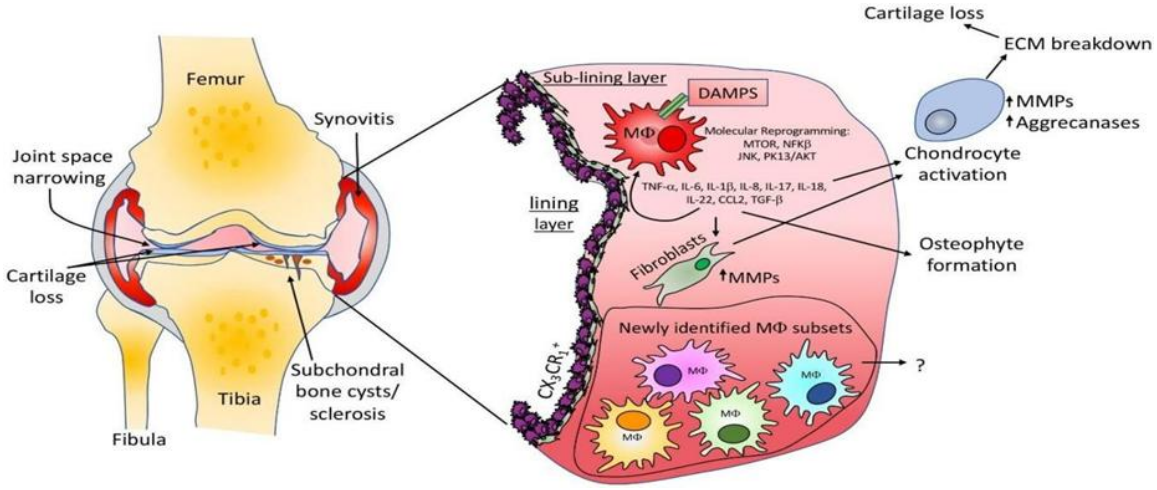


Fig.1.1 Pathogenesis of Knee OA

Clinical manifestations: Crepitus on movement**,** Valgus/ varus deformity**,** Presence of popliteal cyst**,** Popping or crackling sounds with a joint movement**,** Knee Swelling**,** Knee Pain**,** Early morning stiffness (present at least 30min)**,** Joint tenderness**,** Loss of balance or instability**,** Fever**,** Weight loss**,** Anorexia 5&10

Investigations:

- History taking
- Physical examination
- Radiographic imaging includes standing anteroposterior (AP), standing lateral in extension and skyline view of the patella, medial tibiofemoral and patellofemoral joint space narrowing, sub chondral new bone formation, lateral joint space narrowing
- Laboratory findings- erythrocyte sedimentation rate (ESR), c- reactive protein.10,11&12

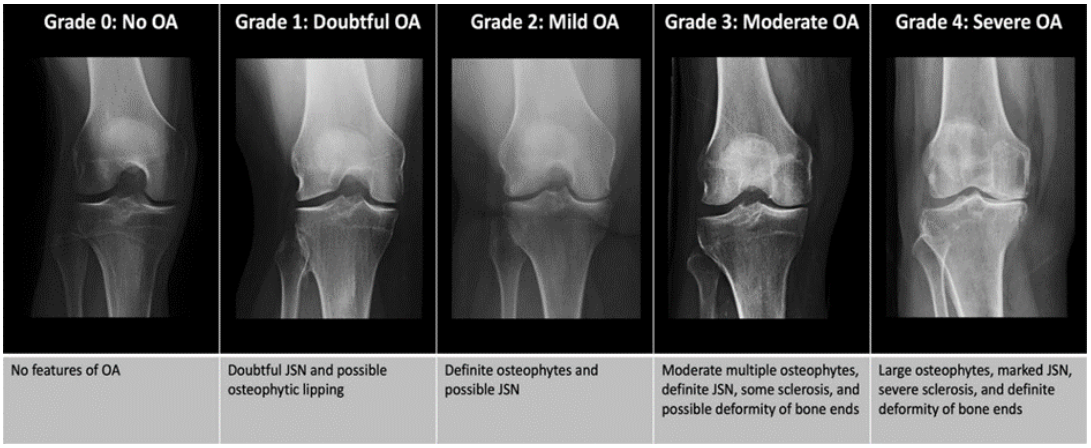


Fig:1.2 Grades of Knee OA

Pharmacological management:

 Platelet-Rich Plasma (PRP): Enhances cartilage repair and reduces inflammation through growth factors and cytokines.

PRP is prepared using a double centrifugation process. Initially, 80 ml of whole blood is collected in tubes with anticoagulants. The first centrifugation is conducted at 3500 rpm for 15 minutes, separating the blood into three layers:

1. Platelet-rich plasma (top layer),
2. White blood cells (buffy coat in the middle),
3. Red blood cells (bottom layer).

A second centrifugation is then performed at 1500 rpm for 7 minutes to remove the platelet-poor plasma (PPP), leaving the lower third as platelet-rich plasma (PRP), which is then used for therapeutic purposes. 13

Hyaluronic Acid (HA): Provides joint lubrication, reduces inflammation, and promotes endogenous HA synthesis.

PRP + Hyaluronic Acid (HA) Hyaluronic acid (HA) is an anionic, non-sulfated glycosaminoglycan composed of repeated units of acetyl glucosamine and D-glucuronic acid. In a normal adult knee joint, 2 ml of synovial fluid contains 2.5-4 mg/mL of HA, with a molecular weight of 5-7 × 10^6 Kd. 14

Synthesis of HA: HA is synthesized by chondrocytes, fibroblasts, and synoviocytes. It is present in synovial fluid and the extracellular matrix (ECM). Injecting HA into the knee joint lubricates the articular surface, reduces wear, nourishes cartilage, and stimulates endogenous HA synthesis, delaying further joint damage.

Mechanism of HA: HA binds to HA-CD44 receptors, decreasing the expression of proinflammatory cytokines like IL and TNF-α. This reduces the production of matrix metalloproteinases (MMPs) 1, 2, 3, 9, and 13, nitric oxide derivatives, and PGE2. It also inhibits disintegrin, preventing the degradation of intra-articular glucosamines and MMPs with thrombospondin motifs. 15,16&17

Complications: Pain, Knee swelling, Stiffness, Reduced movements, Infection, Joint damage, Allergic reactions, Skin discolouration or bruising, Calcification, Haematoma, Nerve injury 4,5&18

Pain and Function Assessment

Visual Analogue Scale (VAS): Used to assess pain severity.

The Visual Analogue Scale (VAS) is widely used for pain measurement due to its simplicity and sensitivity to small changes. It resembles the Numerical Rating Scale (NRS) and the Visual Rating Scale (VRS). The VAS consists of a 10 cm line, with "no pain" on the left and "worst pain" on the right, often represented by a smiling face and a frowning face, respectively. Patients mark a point on the scale that corresponds to their perceived pain level. VAS is commonly recommended for assessing pain severity, monitoring disease progression, and evaluating treatment effectiveness.19&20

WOMAC Index: Measures pain, stiffness, and physical function, widely used for evaluating OA's impact on daily life. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), developed by Bellamy et al., is a validated, self-administered tool for assessing health status in patients with osteoarthritis (OA) of the knee or hip. It evaluates activities of daily living, functional mobility, gait, general health, and quality of life. The WOMAC consists of 24 items divided into three subscales:21,22&23.

1. Pain (5 items):
2. Stiffness (2 items)

3. Physical function (17 items)

II. Aim And Objectives:

- The objective of this research is to study the therapeutic outcomes of PRP+HA.
- To determine/ compare the therapeutic outcome in two subjects receiving PRP and PRP+HA.
- To study the pathological changes based on radiographic imaging (x-ray).
- To provide better evidence in the treatment of knee OA.

III. Materials And Methods:

In This study sample size was 50 by considering all inclusion and exclusion criteria's. 50 subjects were completely treated in the hospital according to the study. the sample size required for the study was calculated by the following formula n=1-96 x px q2d2 n = sample size 1.96 is constant fraction error p = prevalence of previous study q=(1-p) d absolute error Subjects were taken and divided into 2 groups

Study sample size: 50 knee osteoarthritis subjects in two groups

Group-A: receiving PRP alone therapy in grade-2 & grade-3 knee OA (25 subjects).
Group-B: receiving PRP+HA combination in grade-2 & grade-3 knee OA (25 subjects).

Study criteria:
Inclusion criteria:

- Subjects with age group between 30-100 years of both genders.
- Subjects with grade-2 & grade-3 knee OA according to Kellgren- Lawrence grading scale.
- Subjects who are willing to participate in the study and attend to follow-up of minimum 3 visits (1, 3 & 6 weeks)

Exclusion criteria:

- Subjects with past history of trauma or knee surgery.
- Subjects who are taking drugs that inhibit platelet aggregation (NSAIDs, thienopyridines, glycoprotein IIB, IIIA inhibitors, phosphodiesterase inhibitors) in the last seven days.
- Subjects with hypersensitise to HA.
- Subjects with uncontrolled diabetes, pregnancy, breastfeeding, peripheral and vascular diseases, inflammatory arthritis, & metabolic arthritis were excluded from this study.
- Subjects with no major axial deviation (valgus 50, varus 50).

Method of study: It includes demographic data collection, physical examination, past medical history and medication history. Demographic information includes age, gender, weight, affected site (pain on which knee), physical activity.

Physical examinations of the knee including crepitation, range of motion (ROM) flexion and extension were performed at each visit. Differential diagnosis was made among the pathological conditions made in knee OA. Based on radiographic findings x- ray imaging of AP and Lateral view of knee, this gives knee findings this will be analysed based on K&L grading scale. In this prospective observational randomized controlled clinical trial, 50 subjects were agreed to participate and fill their consent form. The study population consist of both genders between 30-70 years of age, with degenerative changes in the cartilage, and osteoarthritis of the knee joint with the grading of II&III as diagnosed by using the Kellgren-Lawrence grading scale. A total of 75 patients participated in this study and 50 patients were included in the study One group received PRP in an aseptic area at the affected site. 3ml of PRP were injected at the affected knee joint. All patients were evaluated at the baseline, 3, 6 weeks after post injection. Another group received PRP+HA combination treatment at the affected site. 3ml+2.5ml were injected at the affected knee joint. All patients were evaluated at the baseline, 3, 6 weeks after post injection. The outcome VAS score (0-10) and WOMAC (96) score measured at follow-up visits.

Statistical analysis: Statistical analysis is done by using Microsoft Excel version 2401 (2021). VAS and WOMAC scores in our study between two groups were compared using Student t. test (T. Test). Standard deviation and mean of VAS and WOMAC score between two groups before and after treatment is calculated. The results of the study were explained in the form of tables, bar diagrams, pie charts. Mean and standard deviation value of the various parameters were calculated. Standard deviation, Mean, P-value of the VAS and WOMAC scores of before and after treatment was calculated using Student t test. The results are shown below tables.

IV. Results:

A Prospective observational comparative study was conducted for 6 months (AUG 2023- FEB 2024) in Orthopaedic unit in Sri Balaji Medical College Hospital and Research Institute, Renigunta, Tirupati. A total of 50 knee OA subjects were categorised into two groups i.e. PRP Group (25 subjects) & PRP+HA Group (25 subjects) based on their type of therapy. We categorized the subjects to their age groups. Out of 50 subjects 19 (38%) of them were from age group 50-59 years followed by 13 (26%) from 40-49 years, 11 (22%) from 60-69 years, 5 (10%) from 30-39 years, 2 (4%) from ≥70 years. Figure5.1. The average age of PRP group male and female subjects is 52 and 51years respectively. The average age of PRP+HA group male and female subjects are 57 and 54 years respectively. We have assessed the occupation status of the study subjects and percentage of others is found to be 20 (40%) followed by teacher 8 (16%), farmer 7 (14%), driver 6 (12%), software 4 (8%), tailor 3 (6%), police 2 (4%) which is explained in the Table 5.2. Out of 50 subjects 24 (48%) were grade II knee OA, in that 16 subjects were given PRP and 8 subjects were given PRP+HA followed by 26 (52) were grade III knee OA, in that 9 subjects were given PRP and 17 subjects were given PRP+HA for the affected knee figure 5.3. Out of 50 subjects 25 were given PRP. VAS scoring after intra articular injection of PRP, before treatment 25 (100%) subjects had severe pain (7-10) and after treatment 19 (76%) subjects had mild pain (1-3) and 6 (24%) subjects had moderate pain (4-6) after PRP treatment. The complete description about score of VAS in both before and after treatment is given in comparative charts are shown in ***Figure 5.4.*** Out of 50 subjects 25 were given PRP+HA. Vas scoring before and after intra articular injection of PRP+HA, before treatment 25 (100%) subjects had severe pain and after treatment 24 (96%) subjects had mild pain, 1 (4%) had moderate pain, The complete description about both before and after treatment is given in comparative charts are shown in ***Figure 5.5.***Out of 50 subjects 25 were give PRP.WOMAC scoring before and after intra articular injection of PRP, before treatment 23 (92%) subjects had extreme pain, 2(8%) had severe pain, and after treatment 17(32%) subjects had severe pain, 8 (32%) had moderate pain.The complete description about both before and after treatment is given in ***Table 6.12*** and comparative charts are shown in ***Figure6.12***Out of 50 subjects 25 were give PRP.WOMAC scoring before and after intra articular injection of PRP, before treatment 18 (72%) subjects had extreme stiffness, 7(28%) had severe stiffness, and after treatment 15(60%) subjects had severe stiffness, 8 (32%) had moderate stiffness,1 (4%) subject had extreme stiffness. The complete description about both before and after treatment is given in ***Table 6.13*** and comparative charts are shown in ***Figure 6.13***Out of 50 subjects 25 were give PRP.WOMAC scoring before and after intra articular injection of PRP, before treatment 21 (84%) subjects had extreme physical function, 4(16%) had severe physical function, and after treatment 19(76%) subjects had severe physical function, 4 (16%) extreme physical function, 2(8%) had moderate physical function. The complete description about both before and after treatment is given in ***Table 6.14*** and comparative charts are shown in ***Figure 6.14***Out of 50 subjects 25 were give PRP+HA.WOMAC scoring before and after intra articular injection of PRP+HA, before treatment 24 (96%) subjects had extreme pain, 1(4%) had severe pain, and after treatment 13(52%) subjects had moderate pain, 12(48%) subjects had severe pain, The complete description about both before and after treatment is given in ***Table6.15*** and comparative charts are shown in ***Figure6.15.***Out of 50 subjects 25 were give PRP+HA.WOMAC scoring before and after intra articular injection of PRP+HA, before treatment 19 (76%) subjects had extreme stiffness, 6(24%) had severe stiffness, and after treatment 23(92%) subjects had moderate stiffness, 1 (4%) had mild stiffness,1 (4%) subject had severe stiffness. The complete description about both before and after treatment is given in ***Table 6.16*** and comparative charts are shown in ***Figure 6.16***Out of 50 subjects 25 were give PRP+HA.WOMAC scoring before and after intra articular injection of PRP+HA, before treatment 23 (92%) subjects had extreme physical function, 2(8%) had severe physical function, and after treatment 18(72%) subjects had severe physical function, 5(20%) subjects had moderate physical function, 2(8%) had severe physical function. The complete description about both before and after treatment is given in ***Table6.17***and comparativechartsareshowninFigure6.1

Fig:5.1 **Age Wise Distribution**

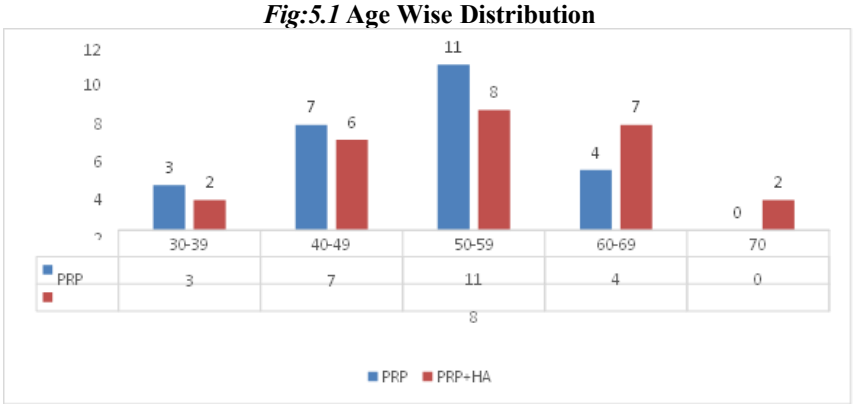


Table 5.2: Distribution Based on Occupation Status

S.NO	Type of Occupation	No. of subjects *(N=50)*	Percentage (%)
1.	Farmer	7	14
2.	Driver	6	12
3.	Software	4	8
4.	Police	2	4
5.	Tailor	3	6
6.	Teacher	8	16
7.	Other	20	40
	TOTAL	**50**	**100**

Figure 5.3: Distribution of Subjects Based on Grades of Knee OA

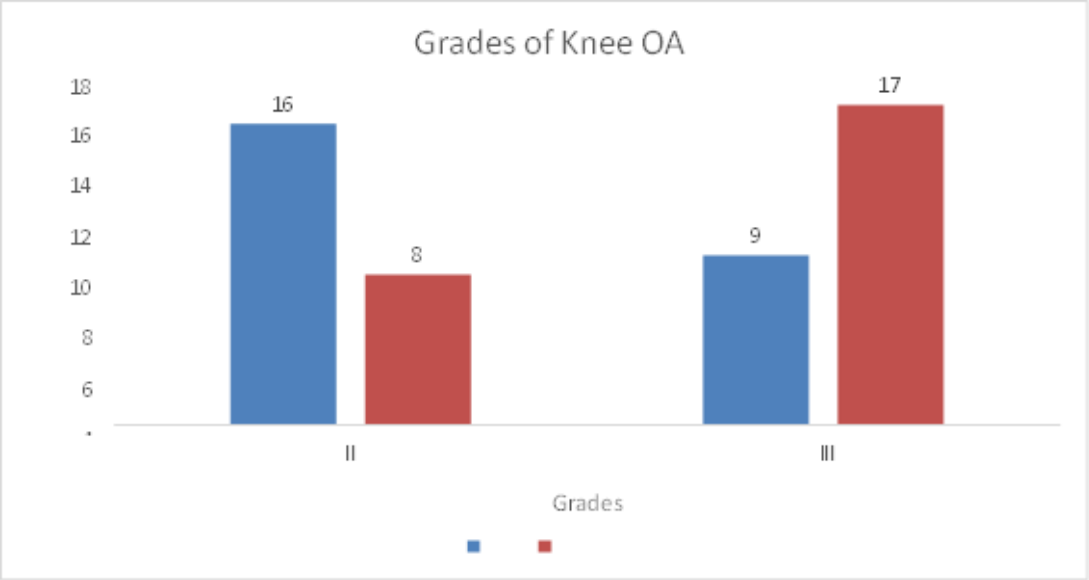


Figure: 5.4 Weight wise Distributions

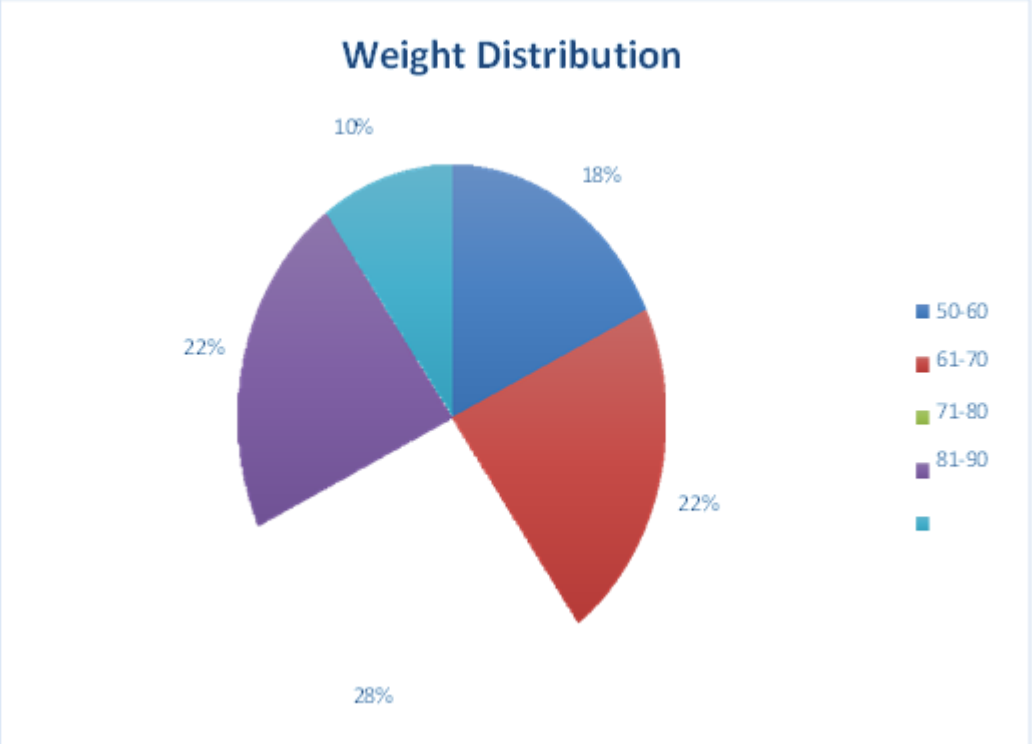
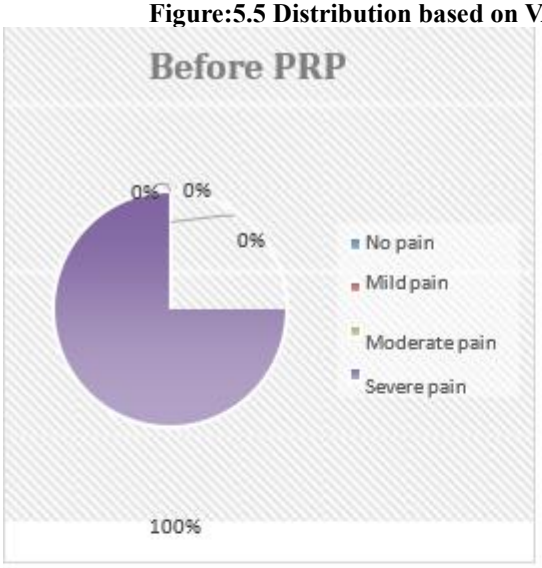


Figure:5.5 Distribution based on VAS scoring before after PRP Therapy



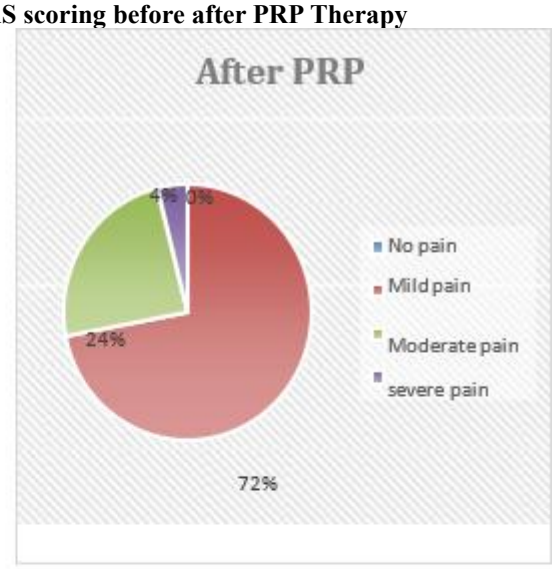
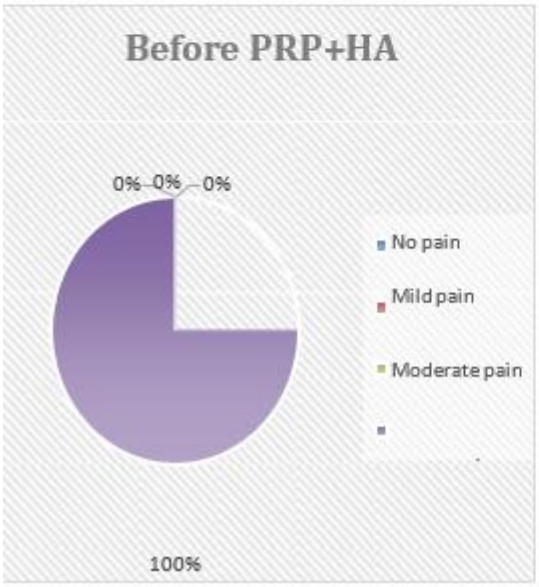


Figure 5.4: Distribution Based on VAS scoring before and After PRP+HA therapy



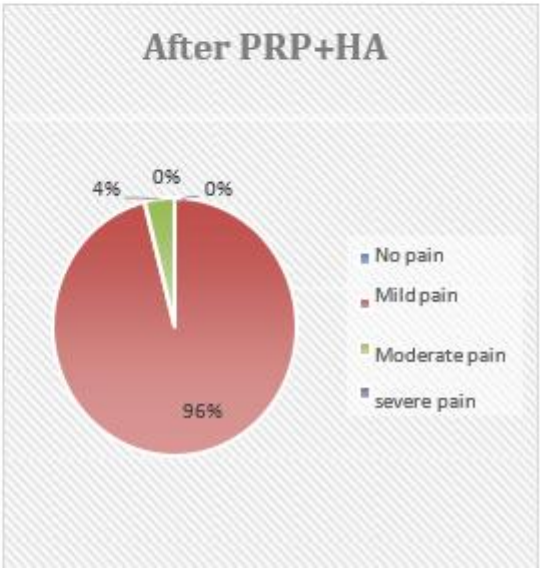


Table 5.5: Individual WOMAC Score Initial PRP Alone & PRP+HA Combination Therapy:

S. No	IP.NO	PRP Group (%)			IP.NO	PRP+HA Group (%)		
		Pain	Stiffness	Physical function		Pain	Stiffness	Physical function
1	0187 MT	18	5	47	0425 MD	10	2	43
2	0138 PM	17	7	57	1568 SU	12	4	42
3	0002 MR	18	6	57	1513 RM	12	5	33
4	0372 AJ	18	8	57	0056 RA	13	6	46
5	0046 BR	12	5	44	2003 MA	9	3	38
6	0022 MB	15	6	52	0127 LB	11	3	36
7	0572 VA	18	7	57	0021 CN	19	7	61
8	4168 HT	19	8	62	0007 SR	11	5	42
9	1693 VD	19	8	60	2132 AS	10	4	48
10	0056 HR	19	8	61	2143 AS	10	4	44
11	8006 AJ	19	7	60	2145 GJ	12	5	58
12	4685 HL	17	8	58	5796 LV	12	5	34
13	0506 PA	19	7	57	4063 AS	11	4	55
14	0048 DK	18	7	46	5614 RG	9	5	41
15	0006 DS	17	8	56	4638 CS	12	5	48
16	0009 AA	17	6	62	8090 SM	9	3	49

17	0066 BK	19	8	62	6004 AK	9	6	55
18	0001 KR	18	6	51	2039 JR	11	5	42
19	4825 TL	19	8	59	2069 PA	9	5	46
20	6735 KC	19	7	57	6540 DS	12	5	45
21	7682 MP	18	8	57	6545 AP	12	5	43
22	1683 MC	19	7	58	3692 MA	13	4	48
23	6782MA	19	7	55	6923 AB	13	5	47
24.	0021 BM	20	6	59	5204 CT	12	5	51
25	4062 PJ	20	8	60	6003 OB	14	6	45
Mean		**18.04**	**7.04**	**56.44**	**Mean**	**18.24**	**7.2**	**59.28**
S. D±		**1.670**	**0.978**	**4.899**	**S. D±**	**1.267**	**0.912**	**4.541**

Table 5.6: Individual WOMAC Score AFTER PRP Alone & PRP+HA Combination Therapy

S. No	PRP group (%)				PRP+HA group (%)			
	Patient.ID	Pain	Stiffness	Physical function	Patient.ID	Pain	Stiffness	Physical function
1	0187 MT	16	5	44	0425 MD	11	2	40
2	0138 PM	19	8	59	1568 SU	6	4	41
3	0002 MR	18	7	62	1513 RM	11	4	32
4	0372 AJ	19	7	57	0056 RA	11	4	45
5	0046 BR	20	8	63	2003 MA	12	4	39
6	0022 MB	20	8	65	0127 LB	10	3	35
7	0572 VA	19	8	61	0021 CN	11	4	60
8	4168 HT	19	8	62	0007 SR	9	4	34
9	1693 VD	19	7	66	2132 AS	10	5	47
10	0056 HR	18	7	57	2143 AS	11	4	42
11	8006 AJ	19	6	58	2145 GJ	11	3	30
12	4685 HL	18	7	59	5796 LV	9	4	32
13	0506 PA	19	8	64	4063 AS	11	4	51
14	0048 DK	18	8	51	5614 RG	10	4	40
15	0006 DS	20	7	62	4638 CS	11	4	47
16	0009 AA	17	6	57	8090 SM	12	3	48
17	0066 BK	17	8	60	6004 AK	9	4	52
18	0001 KR	19	8	63	2039 JR	9	4	40
19	4825 TL	19	8	60	2069 PA	12	4	41
20	6735 KC	18	7	61	6540 DS	9	3	43
21	7682 MP	17	6	60	6545 AP	8	3	42
22	1683 MC	15	8	56	3692 MA	11	4	47
23	6782 MA	17	6	57	6923 AB	7	4	46
24	0021 BM	17	8	58	5204 CT	8	4	50
25	4062 PJ	19	6	60	6003 OB	8	3	34
Mean		**11.48**	**4.64**	**45.6**	**Mean**	**10.12**	**3.72**	**42.32**
S. D±		**2.143**	**1.113**	**6.916**	**S. D**	**1.614**	**0.613**	**7.209**

Statistical Analysis: Table 5.7 VAS SCORE INITIAL AND FOLLOW UP THERAPY

	Initial therapy		Follow up therapy	
	PRP Group	PRP+HA Group	PRP Group	PRP+HA Group
Mean	8.96	9.52	2.84	1.72
SD±	0.789515	0.653197	1.040833	0.791623
P-Value	2.2104		9.5328	

Statistical Analysis: Table 5.8 WOMAC SCORE INITIAL AND FOLLOW UP THERAPY

	Initial PRP Therapy			Follow up PRP		
	Pain	Stiffness	Physical function	Pain	Stiffness	Physical function
Mean	18.04	7.04	56.44	11.48	4.64	45.6
S. D±	1.670	0.978	4.899	2.143	1.113	6.916
P-Value	9.3764	5.0517	2.5476			

Results of student t test: COMPARISION OF VAS SCORES FOR GROUP PRP VS GROUP PRP++HA

GROUP	P-value (95%)
PRP	0.001089**
PRP+HA	

*** Extremely significant **Very significant * Significant

Results of student t test: COMPARISION OF WOMAC SCORES FOR GROUP PRP VS GROUP PRP++HA

GROUP	P-VALUE (95% CI)		
	PAIN	STIFFNESS	PHYSICAL FUNCTION
PRP	0.0047**	0.0002***	0.0086**
PRP+HA			

*** Exremely significant **Very significant * Significant

V. Discussion:

- Most of the studies have suggested PRP+HA combination therapy has shown benefits for knee osteoarthritis patients when compared to PRP alone therapy.
- In our study, by using students t-test between two groups p value for VAS scale is 0.001089, and p value for WOMAC scale pain, stiffness, physical function is 0.00472495, 0.00026514, 0.00862863 respectively. Which shows that strong presumption i.e. p-value <0.05
- We categorized the patients to their age group and found no significant difference in both the groups with p value=0.684423. So, we can compare the results between two groups. The average age of the total study population is 53 years, and the average age of PRP Group and PRP+HA Group is 51 and 55 years respectively. OA is more common in women than men, but the prevalence increases dramatically with age. Nearly, 45% of women over the age of 65 years have symptoms while radiological evidence is found in 70% of those over 65 years, the same was reported by ***Chandra Prakash pal[6], Auiyoun cui et al[7].***
- We observed and confirmed the radiographic imaging findings based on Kellgren- Lawrence grading system of Grade-II &Grade-III is found to be 24, 26 respectively.
- The study is to evaluate the effects of PRP Vs PRP+HA combination therapy on pain, stiffness, physical function of mild-moderate knee osteoarthritis. This study shows the strong presumption on PRP+HA combination therapy. This was already proved by ***Angeline ai ling aw et al.***
- The average and standard deviation of VAS scores for Group-PRP initial and follow up after 6^{th} week is 8.96±0.789515 & 2.84±1.040833 and the average and standard deviation of Group-PRP+HA initial and follow up after 6^{th} week is 9.52±0.653197 &1.72±0.791623.We compare the VAS score for both PRP &PRP+HA and found significance difference p-value=0.001089.
- The average and standard deviation of WOMAC pain, stiffness, physical function scores for Group-PRP initial and follow up after 6^{th} week is 18.04±1.267543556, 7.04±0.978093383, 56.44±4.899659852 & 11.48±2.143206321, 4.64±1.113552873, 45.6±6.91616464 and the average and standard deviation of WOMAC pain, stiffness, physical function scores for Group-PRP+HA initial and follow up after 6^{th}weekis18.24±1.267543556,7.2±0.912870929, 59.28±4.541659021& 10.12±1.614517472, 3.72±0.613731755, 42.32±7.209484494.
- We compare the WOMAC pain, stiffness, physical function scores for both PRP & PRP+HA was found to be significant difference p-value is 0.00472495, 0.00026514, 0.00862863.

VI. Conclusion:

- The current study seems to be focus on comparison of PRP alone therapy Vs PRP+HA combination therapy in Grade-II & Grade-III knee osteoarthritis.
- The results of this research study shows that PRP+HA combination therapy was found to be superior to PRP alone therapy in pain relief, stiffness and physical function improvement for subjects with knee osteoarthritis.
- Performing separate analysis for the VAS scores and WOMAC sub scores for both groups. Comparison showed that PRP+HA has better therapeutic outcome.
- We concluded that PRP+HA combination therapy (synergistic effects) can improve VAS & WOMAC scores (after 6 weeks of treatment) and enhanced benefits in alleviating symptoms and improving joint function.

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