

## FUNCTIONAL OUTCOME OF PATIENTS WITH OSTEOARTHRITIS KNEE TREATED BY INTRAARTICULAR INJECTIONS OF PLATELET-RICH PLASMA

VIKAS KUNTWAD<sup>1\*</sup>, PRAMOD PRALHAD TUPE<sup>2</sup>, AMOL WAGH<sup>3</sup>

Department of Orthopaedics, IIMSR Medical College, Badnapur, Jalna, Maharashtra, India.

\*Corresponding author: Vikas Kuntwad; Email: vikaskuntwad@gmail.com

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### ABSTRACT

**Objectives:** The aims and objectives of the study are (1) to assess pain relief and functional outcome in knee osteoarthritis (OA) cases treated by intra-articular injection of platelet-rich plasma (PRP) and (2) to study the complication in patients treated by intra-articular injection of PRP.

**Methods:** This was a prospective study conducted in the department of orthopedics of a tertiary care medical institute. 60 patients with Grade 2 and Grade 3 OA of knee were included in this study on the basis of a pre-defined inclusion and exclusion criteria. All patients were treated by intra-articular injection of PRP. Patients were followed up for 6 months. During follow-up visits, assessment of severity of pain and functional outcome was done by Visual Analog Scale (VAS) Score and Japanese Orthopedic Association (JOA) Score. Patients were also assessed for complications.  $p < 0.05$  was taken as statistically significant.

**Results:** Out of 60 studied cases, there was a female preponderance with a M: F ratio of 1:0.62. The mean age of affected cases was found to be  $65.84 \pm 11.86$  years and mean duration of symptoms was found to be  $2.52 \pm 1.26$  years. Majority of the patients were either overweight (45.00%) or obese (36.67%) and only 11 (18.33%) patients had a healthy weight. 38 (63.33%) patients were having Grade 3 OA whereas 22 (36.67%) patients were having Grade 2 OA. There was a significant reduction in pain and significant functional improvement at the time of final follow-up as compared to VAS and JOA scores at the time of presentation ( $p < 0.0001$ ). Complications were seen in any of the cases.

**Conclusion:** Patients with Grade 2 and Grade 3 OA of knee treated by intra-articular injection of PRP show excellent outcome in terms of pain relief and functional outcome with no significant complications.

**Keywords:** Knee osteoarthritis, Intra-articular injection, Platelet-rich plasma, Functional outcome.

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### INTRODUCTION

Osteoarthritis (OA) of the knee represents a common cause of frequent orthopedic consultations. It is also responsible for a significant burden on both individuals and health-care systems [1]. This degenerative joint disorder is characterized by progressive deterioration of articular cartilage, leading to pain, impaired mobility, and reduced quality of life for millions of individuals worldwide. In India, where the prevalence of knee OA is steadily increasing due to factors such as an aging population and evolving lifestyles, the impact of this condition has already gained significant proportion [2].

Patients with OA knee often present with persistent pain, stiffness, and reduced mobility [3]. The hallmark radiological modality for assessing knee OA remains conventional X-rays, which shows features such as joint space narrowing, osteophyte formation, and subchondral sclerosis. More advanced imaging techniques such as computed tomography and magnetic resonance imaging can show details of soft-tissue involvement, including cartilage integrity and ligamentous structures [4].

Addressing the challenges posed by knee OA demands a wide array of treatment options, spanning from conservative methods such as physical therapy and medication, such as non-steroidal anti-inflammatory drugs to more invasive surgical procedures such as osteotomies and knee replacement surgeries [5]. Among these choices, intra-articular injections of platelet-rich plasma (PRP) have garnered significant attention as a potential solution for pain relief, enhanced

function, and potential disease modification. PRP, a concentrated source of growth factors obtained from a patient's own blood, holds promise for promoting tissue healing and regeneration [6]. Although there is an exponential increase in the number of studies being undertaken to assess the outcome of patients with knee OA treated by PRP, there are considerable gaps in our knowledge regarding its effectiveness, safety, and long-term outcomes. Understanding the factors influencing the functional outcomes of patients undergoing PRP treatment is critical. It is essential to ascertain the extent to which PRP injections can serve as a viable alternative to more invasive interventions [7].

Till, recently, intra-articular injection of steroid was commonly used for pain relief in cases of knee OA. Steroid injections are known for their potent anti-inflammatory properties. These injections offer quick relief from pain and inflammation, often resulting in immediate symptomatic improvement [8]. However, the effects of steroid injections are usually short-lived, and they do not address the underlying structural changes in the joint associated with OA. On the other hand, PRP injections harness the regenerative potential of the patient's own blood, delivering a concentrated source of growth factors that can potentially stimulate tissue repair and cartilage regeneration. It offers the advantage of promoting long-term healing and modifying the disease progression, rather than merely providing symptomatic relief [9]. Researchers are increasingly inclined toward PRP over steroid injections because of its potential to address the root causes of knee OA, rather than just providing temporary relief. PRP injections align with the growing trend in regenerative medicine, focusing on enhancing tissue repair and functional recovery, which can significantly benefit patients in the

long term. This shift in focus from symptomatic management to disease modification is a key driver behind the growing interest in PRP as a treatment option for knee OA [10].

We conducted this study to analyze the functional outcomes of knee OA patients treated by intra-articular injections of platelet-rich plasma, exploring its potential as a less invasive therapeutic approach for this debilitating condition.

## METHODS

This was a prospective study conducted in the department of orthopedics of a tertiary care medical college. 60 patients with knee OA not responding to pharmacological treatment for more than 6 months were included in this study on the basis of a pre-defined inclusion and exclusion criteria. Informed and written consent to be part of the study was obtained from all the participants. To determine the sample size, we used OPENEPI software version 3. We calculated the sample size based on the findings from a preliminary pilot study done on the subject of knee OA with the aim of achieving 90% statistical power and a 95% confidence level. According to the principles of the central limit theorem, a sample size exceeding 55 was considered sufficient, so we included 60 patients in our study.

Demographic details of patients such as age, gender, and socioeconomic status and area of residence were noted. Weight, height, and body mass index of all the patients were also noted. A detailed history with respect to affected side (right, left, or both), duration, as well as severity of symptoms along with type of previous treatment was also asked and noted. The patients were also assessed for functional disability consequent upon knee arthritis by asking them about difficulty in routine daily activities such as kneeling, squatting, and using stairs. A thorough clinical examination was done with an aim to evaluate presence of joint tenderness, crepitus, and signs of inflammation such as redness and swelling. Range of motion and joint stability were also assessed. Imaging studies in the form of X-ray of both knees (AP weight-bearing view) were done in all cases. Computed tomography and magnetic resonance imaging were done in selected cases in whom knee instability was suspected. The severity of OA was graded as per Kellgren and Lawrence system for classification of OA [11] (Table 1).

Routine investigations such as complete blood count, renal function test, coagulation profile, hepatic function tests, HBSAg, and HIV. All patients received intra-articular injection of PRP.

### Technique of PRP injection

40 mL of patient's venous blood was collected by venipuncture in acid citrate dextrose sterile tubes. These tubes were then spun at 2000 rpm for 5 min. Supernatant fluid thus formed was then collected into a 10 mL sterile tube. This 10 mL supernatant fluid was again centrifuged for 10 min. The lower 1/3<sup>rd</sup> of the content formed as a result of this second centrifugation was then collected.

This PRP was then injected into the affected knee by lateral approach with all aseptic precautions. After injection, patient was instructed to keep the knee in flexed position for 15 min to ensure proper distribution of PRP throughout the affected knee. Patients were discharged on the same day with an instruction to take analgesic and cold packs if required. All patients received 3 PRP injection 1 month apart.

Patients were followed up and assessed every monthly from the day of first injection till 6 months. During each follow-up visit, patients were assessed for severity of pain and functional ability by Visual Analog Scale (VAS) score and Japanese Orthopedic Association (JOA) score.

Statistical analysis was done using SPSS version 21.0 software. Quantitative data were presented as mean and standard deviation. For quantitative data, unpaired t-test was applied and for qualitative data, Chi-square test was used.  $p < 0.05$  was taken as statistically significant.

### Inclusion criteria

1. Patients with Grade 2 and Grade 3 OA as per Kellgren and Lawrence system for classification of OA
2. Age above 18 years
3. Not responding to non-invasive treatment for more than 6 months
4. Ready to give written informed consent to be part of study.

### Exclusion criteria

1. Those who refused consent
2. Age <18 years
3. Pregnant women
4. Those who received oral steroids or chemotherapeutic agents for arthritis or for any other reason
5. Patients with progressive polyarticular arthritis such as secondary to rheumatoid arthritis, systemic lupus erythematosus, and gout.

## RESULTS

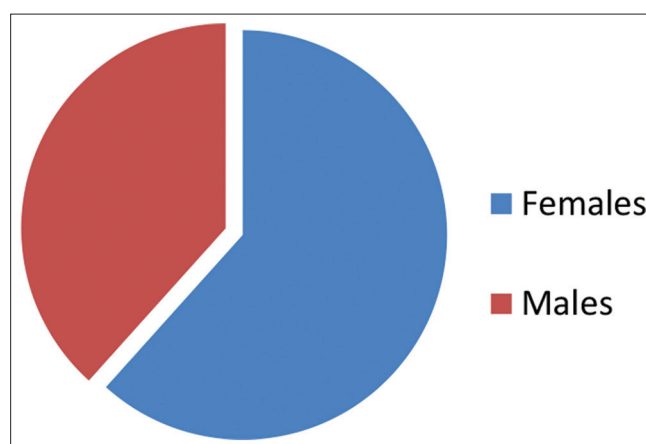
60 adult patients with knee arthritis were included in this study. Out of 60 cases, 37 (61.67%) were females and 23 (38.33%) were males with a M: F ratio of 1:0.62 (Fig. 1).

The analysis of the patients on the basis of duration of symptoms showed that most of the patients had symptoms for 2–3 years (53.33%) followed by more than 3 years (21.67%), 1–2 years (15.00%), and <1 year (10.00%). Mean duration of symptoms was found to be  $2.52 \pm 1.26$  years (Table 2).

The most common affected age group was above 60 years (48.33%) followed by 51–60 years (35.00%) and 41–50 years (13.33%). Only 2 (3.33%) patients were below 40 years of age. The mean age of affected cases was found to be  $65.84 \pm 11.86$  years (Table 2).

**Table 1: Grades of osteoarthritis knee Kellgren and Lawrence classification**

Grade	Imaging features
Grade 0 (none)	Definite absence of X-ray changes of osteoarthritis
Grade 1 (doubtful)	Doubtful joint space narrowing and possible osteophytic lipping
Grade 2 (minimal)	Definite osteophytes and possible joint space narrowing
Grade 3 (moderate)	Moderate multiple osteophytes, definite narrowing of joint space, and some sclerosis and possible deformity of bone ends.
Grade 4 (severe)	Large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone ends.



**Fig. 1: Gender distribution of studied cases**

Out of 60 cases, majority of the patients were either overweight (45.00%) or obese (36.67%) and only 11 (18.33%) patients had a healthy weight. The grading of severity of OA showed that out of 60 cases, 38 (63.33%) patients were having Grade 3 OA whereas 22 (36.67%) patients were having Grade 2 OA of predominantly affected knee (Table 3).

Assessment of severity of pain in studied cases showed that at the time of presentation, there was moderate to severe pain experienced by all patients. The mean VAS score at the time of first presentation was found to be 8.26±3.90. After intra-articular injection of PRP, the severity of pain gradually reduced and at the time of final follow-up, the mean VAS score was found to be 1.22±0.74. There was a considerable decrease in severity of pain in almost all patients and this decrease was found to be statistically highly significant (p<0.0001). Similarly, during each follow-up, patients were assessed for functional outcome on the basis of JOA scores. At the time of presentation, mean JOA score was found to be 41.12±18.80. A gradual increase in mean JOA score was observed during each follow-up visits and at the time of final follow-up, the mean JOA score was found to be 84.36±12.74. There was a statistically significant improvement in mean JOA scores of the cases over the follow-up period of 6 months (p<0.0001) (Fig. 3).

There were no significant complications in any of the studied cases.

**DISCUSSION**

In our study of OA knee treated by intra-articular injection of PRP, females were found to be predominantly affected. While multiple

factors contribute to the increased prevalence of OA in females compared to males, recent research suggests an interplay of biological, genetic, hormonal, and lifestyle factors. Some studies have highlighted the role of estrogenic, which is known to influence cartilage metabolism and may contribute to increased susceptibility in women [11]. Not only OA is more common in females but also some studies have also suggested that women having OA often have more severe pain and more profound reduction in function and quality of life as compared to men. Pal et al. conducted an epidemiological study aimed at determining the prevalence of primary knee OA [12]. For this purpose, five diverse sites, representing various urban and rural settings, were covered, with a total sample size of 5000 subjects. The findings revealed an overall knee OA prevalence of 28.7%, with notable factors associated with its occurrence being female gender, obesity, increasing age, and engagement in sedentary work. Similar propensity for females to develop OA knee was also reported by the authors such as Davis et al. [13] and Sharma et al. [14].

In our study, the most common affected age group was found to be individuals above 60 years of age (48.33%). Along with, aging obesity and being overweight were also found to be one of the risk factors for the development of OA of knee joints. With advancing age, there is a cumulative effect of joint wear and tear as well as the gradual deterioration of articular cartilage and other joint structures. Genetic predisposition and metabolic changes that occur with aging may also play a role in the development of OA. In addition, age-related conditions such as obesity, decreased physical activity, and comorbidities can further exacerbate joint degeneration that is the underlying cause of OA. Shane Anderson and Loeser in their review showed that the age-related changes in the musculoskeletal system play a significant role in increasing the susceptibility to OA [15]. These factors encompass joint injuries, obesity, genetic predisposition, and anatomical features that influence joint mechanics. The authors further found that natural aging process also contributes to the development of OA by introducing changes in joint tissues. This includes cell senescence, which leads to the development of the senescent secretory phenotype, as well as alterations in the joint matrix, such as the formation of advanced glycation end-products that affect the mechanical properties of joint tissues. The authors concluded that given the aging population and the rising prevalence of OA risk factors like obesity, the ability to impede OA progression in older adults holds significant public health implications. Similar age-related changes in joints, particularly load-bearing joints, have also been reported by the authors such as Loeser [16] and Hawker and King [17].

In our study, there was an excellent outcome in terms of reduction in pain as well as functional improvement in cases treated by intra-articular injection on PRP. There was a considerable decrease in severity of pain and improvement in functional outcome in almost all patients and this change was found to be statistically highly significant

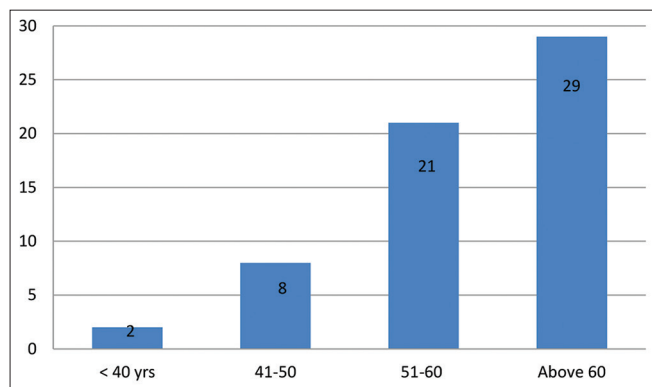
**Table 2: Mean duration of symptoms in studied cases**

Duration of symptoms	No of patients	Percentage
<1 year	6	10.00
1-2 years	9	15.00
2-3 years	32	53.33
>3 years	13	21.67
Total	60	100.00

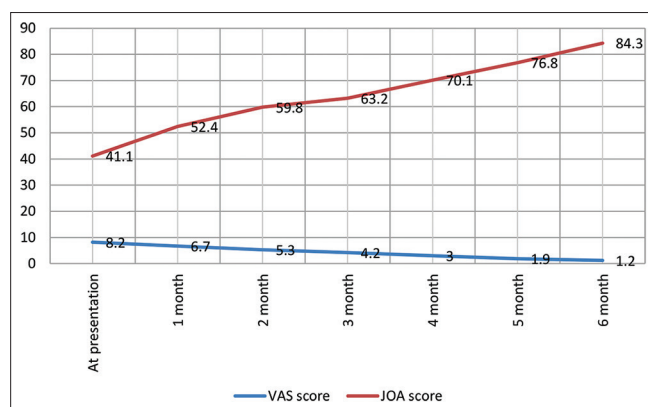
Mean duration of symptoms=2.52±1.26 years

**Table 3: Body mass index in studied cases**

Body mass index and severity of osteoarthritis	Number	Percentage
Body mass index		
Healthy weight (18.5-24.9)	7	18.33
Overweight (25-29.9)	32	45.00
Obese (30 or above)	11	36.67
Total	40	100.00
Grade of osteoarthritis as per Kellgren and Lawrence system		
Grade 2	22	36.67
Grade 3	38	63.33
Total	60	100



**Fig. 2: Age distribution of studied cases**



**Fig. 3: Visual analog scale and Japanese orthopedic association scores over the period of 6 months**

( $p < 0.0001$ ). Filardo *et al.* conducted a review study to evaluate effectiveness, in terms of patient-reported outcome measures, of PRP injections for knee OA compared to placebo and other intra-articular treatments [18]. For this purpose, the authors studied 34 randomized controlled trials, including 1403 knees in PRP groups and 1426 in control groups. The authors found that patients treated by PRP were having better outcome as assessed by Western Ontario and McMaster Universities OA Index with a statistically and clinically significant difference versus placebo at 12-month follow-up ( $p = 0.02$ ) and versus HA (hyaluronic acid) at 6-month ( $p < 0.001$ ) and 12-month ( $p < 0.001$ ) follow-ups. A clinically significant difference favoring PRP versus steroids was documented for VAS pain ( $p < 0.001$ ), Knee Injury and OA Outcome Score pain ( $p < 0.001$ ), function in daily activities ( $p = 0.001$ ), and quality of life ( $p < 0.001$ ) at 6-month follow-up. On the basis of these findings, the authors concluded that the effect of platelet concentrates goes beyond its mere placebo effect, and PRP injections provide better results than other injectable options. Similar outcome in patients of OA knee treated by PRP was also reported by the authors such as Dong *et al.* [19] and Dai *et al.* [20].

## CONCLUSION

Intra-articular injections of PRP for patients suffering from moderate to severe knee OA have yielded notable positive outcomes. Patients treated by intra-articular injection of PRP have shown significant enhancements in functional outcomes and a significant reduction in the severity of pain. Importantly, the use of PRP injections has also been associated with negligible complication rates, further underlining its potential as a valuable therapeutic option for individuals afflicted by knee OA.

## CONFLICT OF INTEREST

None.

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