

## Original Research Article

# Clinical outcome of early-stage knee osteoarthritis after intra-articular platelet rich plasma injection

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## ABSTRACT

**Background:** Osteoarthritis (OA) is a degenerative joint disease due to degradation of articular cartilage, proliferative reformation of subchondral bone and low degree of synovitis resulting in reduced quality of life (QOL), being the major cause of pain and disability in the elderly population. Platelet-rich plasma (PRP) is an autologous mixture of concentrated platelets and growth factors produced by centrifugation of whole blood, used to treat bone, tendon and ligament injuries. The growth factors released by PRP have been shown to promote cell recruitment, proliferation and angiogenesis resulting in a decrease in the expression of inflammatory enzymes. The aim was to study the effectiveness of intra-articular PRP injections in early-stage OA knee patients and to evaluate the clinical outcome and QOL at 6 months.

**Methods:** We conducted an observational study of 100 patients with early OA knee changes with age group >50 years and injected their knees with PRP injections and serial follow up assessment was done.

**Results:** We saw significant improvement in quality of lives evaluated as per world health organization quality of life (WHOQOL) questionnaire after PRP injections on their follow-up. Significant reduction in pain, reduction in joint stiffness and improvement in physical activities shown by significant reduction in Western Ontario and McMaster universities osteoarthritis index (WOMAC) scores.

**Conclusions:** OA of knee is one of the commonest rheumatological problems after 50 years of age. It was commonly observed in females more than 60 years age with sedentary lifestyle. PRP therapy has given excellent results in pain relief, reduction of joint stiffness and improvement in physical activities and improvement in QOL.

**Keywords:** OA, PRP, Knee joint, QOL

## INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease due to degradation of articular cartilage, degradation and proliferative reformation of subchondral bone and a low degree of synovitis that results in reduced QOL (QOL). OA is one of the major causes of pain and disability in the elderly population (>70 years).<sup>1</sup> OA alters the normal joint metabolism promoting increased catabolism and decreased anabolism. Inflammation, in combination with cell death, meniscal changes, bone remodelling and

subchondral sclerosis, produces a vicious cycle of progressive joint degeneration. This can be accentuated by excessive mechanical stress and oxidative damage. Under certain conditions like metabolic or cytotoxic stress, such as in ageing, autophagy can be upregulated, further decompensating homeostatic mechanisms.

In OA knees, chondrocyte senescence and loss of cartilage integrity are prominent features. There is a surge in the water content of hyaline cartilage, accompanied by decrease in corresponding proteoglycan concentration,

length and aggregation, causing cartilage stiffness and fibrillation of the cartilage surface. From this stage, cartilage proceeds to erode resulting in deep clefts. Concurrently, subchondral bone shows morphological changes. The synovial fluid infiltrates into subchondral bone causing the formation of subarticular cysts. Osteophytes (bony projections) are characteristic features of knee OA in non-pressure areas, caused due to the flattening of bone from pressure in high-wear areas.<sup>2</sup>

OA is listed as the second most common rheumatologic problem and crowned as most frequent joint disease with a prevalence of 22% to 39% in India. OA is more prevalent in women than men, but the prevalence increases dramatically with age. Nearly, 45% of women above the age of 65 years have symptoms while radiological evidence is found in 70% of those above 65 years. OA of knee is considered as a major cause of mobility impairment, particularly among females. OA is evaluated to be the 10<sup>th</sup> leading cause of nonfatal burden.<sup>3,4</sup>

Many factors play an interacting role in indicating the potential for the development of knee OA, although age is typically highlighted. Primary care databases from most of the countries have shown a higher incidence of knee OA than hip or hand OA and a progressive increase in new knee OA cases in the past decade, especially in 35-44-year-olds. Over a 7-year period, an estimated 13% of adults above 50 years receive a diagnosis of OA with the knee joint implicated in 25% of the population. There is also an associated socio-economic burden in terms of cost of medical care for both government and individuals. It is a major public health problem worldwide and is expected to rapidly increase as the age of population rises and rates of obesity escalate.<sup>1</sup>

### ***Current strategies in knee OA management***

Knee OA management strategies include improvement in function, reduction in disability, pain relief and hence, improved QOL. However, there is no pharmacologic agent available to halt OA progression or to reverse existing damage. Existing approaches focus on preventing or delaying progression by developing less invasive procedures or applying interventions earlier in the disease onset. Non-operative therapeutic interventions involving intra-articular injection at the knee joint, including hyaluronic acid (HA), corticosteroids, PRP, non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy and unloaded bracing, play major roles in the management of knee OA.<sup>5</sup>

PRP is an autologous mixture of highly concentrated platelets and associated growth factors and other bioactive components produced by centrifugal separation of whole blood, which is used in orthopaedic and sports medicine practices to treat bone, tendon and ligament injuries.<sup>5</sup> The growth factors released by PRP have been shown to promote cell recruitment, proliferation and angiogenesis resulting in a reduction in the critical regulators of the

inflammatory process and a decrease in the expression of inflammatory enzymes. PRP may induce a regenerative response by improving the metabolic functions of damaged structures, and has been shown to have a positive effect on chondrogenesis and mesenchymal stem cell proliferation.<sup>8-10</sup>

The supra-physiological release of platelet-derived factors directly at the site of cartilage disease, particularly with interest to knee OA, may stimulate the natural regenerative signalling cascade and enhance the healing of tissue with further mediation of the anti-inflammatory response. In OA joints, PRP has been shown to affect local and infiltrating cells, mainly synovial cells, endothelial cells, those cells involved in innate immunity (such as macrophages) and cartilage and bone cellular components.<sup>11</sup>

The combined effects of PRP make it a potential option for management of knee OA, especially as a primary analgesic agent. This is due to an increase in proliferation of tenocytes, osteoblasts and mesenchymal stem cells resulting in decreased pain levels postoperatively.<sup>7</sup>

The aim of our research was to study the effectiveness of intra-articular PRP injections in early-stage OA patients and to evaluate the clinical outcome and QOL at 6 months.

## **METHODS**

Our study was an Observational study designed as a descriptive longitudinal type carried out over a period of two years from October 2018 to September 2020.

The study included a total of 100 patients with clinically and radiologically diagnosed OA of knee joint/ joints with age of 50 years and above coming to the outpatient department of orthopaedics at Pravara rural hospital, Loni.

The patients included in the study included those with age 50 years and above; with complaints of painful knees for more than 6 months; ready to give consent for injecting PRP injection in the affected knees.

Ethical committee approval and written informed consent of the study subjects was taken prior to commencement of the study.

Patients with active infective pathology around the knee joint, on anti-coagulant therapy or with bleeding disorders, platelet functional and morphological disorders, any primary or secondary malignancies, severely anaemic, uncontrolled diabetes mellitus, and OA other than knee joints were excluded from our study.

All the study subjects underwent a common protocol of management. After proper informed consent and history taking, clinical assessment was done. Severity of symptoms were assessed by WOMAC score, the patients were explained about the procedure and the risks

associated with it. For the preparation of PRP, 10 mL of peripheral blood was collected maintaining strict sterility protocol. The collected blood underwent a series of centrifugation process with 3000 rotations per minute for 10 to 12 minutes, thereby delivering the desired PRP with four- to six-fold increase in platelet concentration. Intra-articular administration of PRP was done by injecting 5 mL of platelet concentrate in the supra-patellar pouch through supero-lateral approach with a 22-gauge needle. No form of local anaesthetic was used. Immediately after the injection, passive flexion and extension of the affected knee was performed.

The patients were observed for 30 minutes, following which they were given injection paracetamol for pain on "SOS basis" and prophylactic oral antibiotics for 3 days. They were instructed to limit the use of their affected knee for 24 hours. The patients were especially instructed not to use any/asked to stop medications 48 hours before the follow-up assessment.

The patients were followed up for reduction in pain, reduction in stiffness and improvement in physical function in accordance with WOMAC scoring system on (pre-procedure) day 0 and (post-procedure) at the end of 6<sup>th</sup> week, 3<sup>rd</sup> and 6<sup>th</sup> months and QOL in accordance with WHOQOL questionnaire before PRP therapy and at the end of 6<sup>th</sup> month.

WOMAC consisted of a questionnaire which is aimed to assess three items in subscales of 0-4 containing total of 24 questionnaires. 1. Pain severity during different situations-5 questionnaire, 2. Severity of joint stiffness-2 questionnaire, 3. Difficulty in performing daily functional activities-17 questionnaire.

All the recorded data were subjected for statistical analysis. SYSTAT version 12 (made by Crane's software, Bangalore) was used to carry out the statistical analysis. None of the patient in our study group developed any major complication or local infection.

## RESULTS

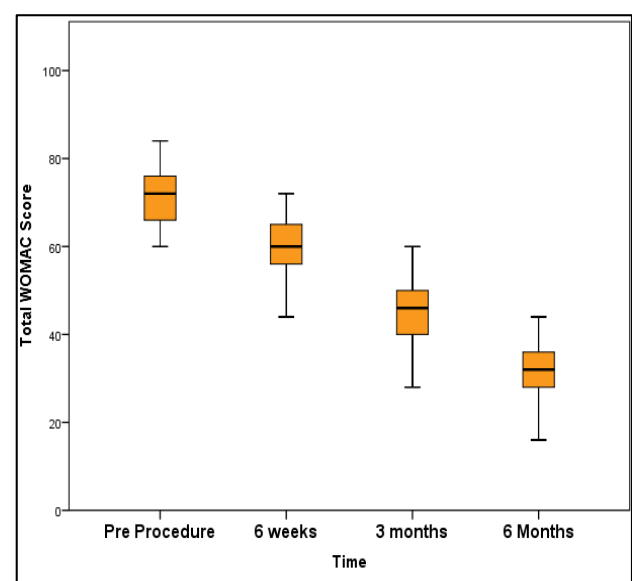
### *Clinical outcome*

In a study conducted by Mohammed et al in 55 patients with knee OA treated with PRP showed a significant improvement in pain and function in terms of WOMAC scores from baseline.<sup>12</sup>

In a comparative study conducted by Ramesh et al between autologous platelet rich plasma therapy and corticosteroid injection for the patients with early knee OA. The patients showed improved range of movements with superior  $p < 0.001$  for VAS, WOMAC and KOOS score which was statistically significant than corticosteroid injection. Autologous PRP injection was stated 89.78% effective in patients with early knee OA.<sup>13</sup>

In a study conducted by Naresh Kumar et al in 2017 in 50 patients with knee OA showed improvements in functional outcome measured in terms of VAS and WOMAC scores which shown a statistically significant outcome with  $p$  value of 0.001. They concluded that PRP showed a significant improvement in pain and functional status of knee at 1, 3 and 6 months after single intra articular PRP injection.<sup>14</sup>

In our study we observed significant reduction in pain, reduction in joint stiffness and improvement in physical activities as shown by significant reduction in WOMAC score values at each successive follow-ups with mean WOMAC scores of 60, 46 and 32 at 6 weeks, 3 months and 6 months respectively post PRP therapy. We observed significant mean differences in mean values with  $p < 0.001$ .



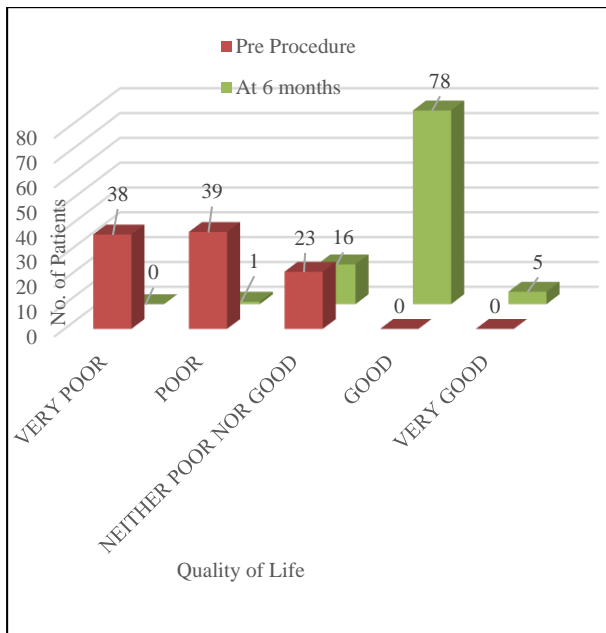
**Figure 1: Change in WOMAC score over time.**

### *Quality of life*

In a study conducted by Wang-Saegusa et al evaluated the effects of plasma-rich growth factor (PRGF) on function and QOL of patients with knee OA and reported that the mean changes of WOMAC and related parameters and mean changes of physical parameters of SF-36 questionnaire for QOL were meaningful.<sup>15</sup>

In a study conducted by Raeissadat et al concluded that intra-articular knee injection of PRP can decrease joint pain and stiffness and improve patients' QOL in short term and can be used as alternative therapy in selective patients resistant to current nonsurgical treatments.<sup>16</sup>

In our study of 100 patients 38 had very poor, 39 had poor and 1 had neither poor nor good QOL before PRP injection evaluated by WHOQOL. At 6 months post PRP therapy 5 had very good, 78 had good, 16 had neither good nor poor and 1 had poor QOL which showed highly significant improvement in QOL with  $p < 0.001$ .



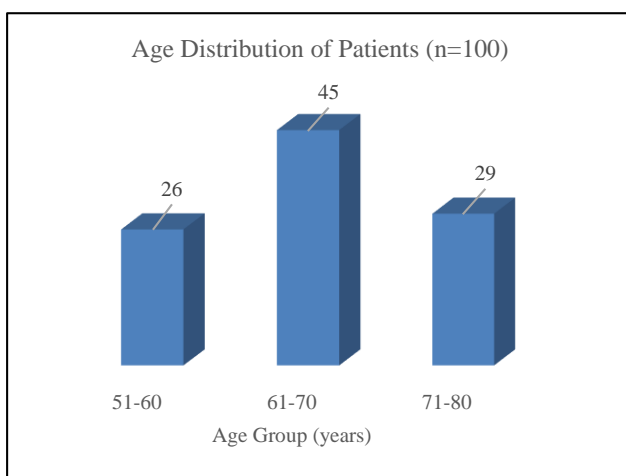
**Figure 2: QOL before and after the procedure.**

#### Distribution of age and sex

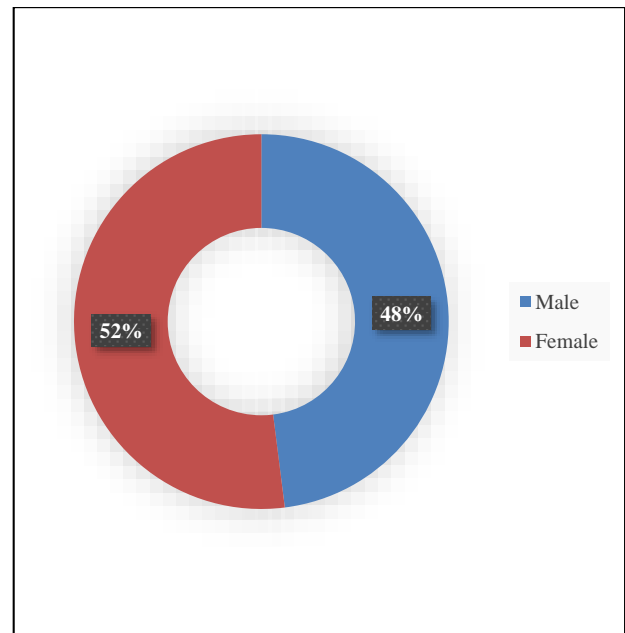
According to studies by Felson et al showed x-ray evidence of OA had increased with age, from 27% in subjects with age less than 70 years, to 44% in subjects aged 80 years and above. There was a slightly higher prevalence of x-ray changes of OA in women than in men (34% versus 31%). However, there was a significantly higher proportion of women with symptomatic disease (11% of all women versus 7% of all men;  $p=0.003$ ).<sup>17</sup>

In a study conducted by Akinpelu et al indicated high prevalence of knee OA in women than in men. The ratio had been 1.2:1 between women and men.<sup>3</sup>

In our study of 100 patients 52 were females and 48 were males, with the mean age of 66 years (range 50 to 80 years) with the most common age group being 61 to 70 years.



**Figure 3: Age distribution of patients.**



**Figure 4: Sex distribution.**

#### DISCUSSION

In a rapidly developing world where technologies have progressed to make artificial intelligence capable of controlling devices, automobiles and instruments with the mobile phones, making the people adapt to more sedentary life which has shifted our health care from communicable to non-communicable diseases.

The so-called epidemic modernisation together with increasing average life span of humans has contributed to the increasing cases of OA of knee.

OA being a progressive degenerative and one of the oldest diseases in mankind still lacks a definite therapeutic or pharmacological agent to treat or stop the progression other than total knee replacement.

Before opting for total knee replacement patients undergo a variety of non-surgical treatment modality for the relief of symptoms.<sup>18</sup>

Increased understanding of anatomy, pathophysiology and biochemical events occurring at the articular cartilage has led to invention of novel methods in treatment of OA knee lately.

One among them is PRP therapy, which has gained popularity in the last decade worldwide mainly due to its promising results, easy availability, fewer complications and at affordable cost.

Despite being one of the promising modalities of treatment in knee OA it still lacks conclusive evidence to support the theory of a regeneration of substantial or irreversible cartilage damages by PRP therapy.<sup>19</sup>



Our study included 100 patients with early-stage knee OA (Kellgren Lawrence grade 0-2 based on x ray findings) and given a single intraarticular injection of autologous platelet rich plasma and the outcomes of whom were assessed pertaining to improvement in their QOL and well-being.

### Limitations

The assessment of patients beyond 6 months and long-term follow-up were out of the scope of this study. Patients with multiple co-morbidities and internal derangements of the knee with previous history of intra articular tibial plateau fractures or ligament injuries (operated / non operated) were not considered in our study.

Patients diagnosed with advanced arthritic changes in the knees on x-rays were not considered in our study, as India being a developing country, with most of the patients coming to our healthcare facility with lower socio-economic groups with did not consider health as a significant aspect of their lives until severely symptomatic landed up with advanced grade OA knees and could not considered ideal candidates for PRP injections and more indicated for operative intervention.

Majority of the patients coming to our health care facility belonged to daily wage worker groups and did not consent to our methods even after being thoroughly counselled but rather considered non-allopathic management techniques due to their non-belief in newer advances in science and irrational behaviour.

### CONCLUSION

OA of knee is one of the commonest rheumatological problems after 50 years of age. The youngest patient in our study was 51 years of age while the eldest was 80 years old, with the mean age being 66 years.

OA knee was commonly observed in female patients with age more than 60 years with more sedentary lifestyle.

There were no major complications or incidences of local infection in our study group.

PRP therapy has given excellent results in pain relief, reduction of joint stiffness and improvement in physical activities and improvement in QOL at end of 6 months.

Hence, PRP therapy can be used in management of early-stage knee OA to provide relief from symptoms and to improve QOL with negligible complication, low cost and ultimately with good results. Outcome of treatment depends on age, sex and stage of the disease and the inherent potential of the articular cartilage to regenerate.

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*Ethical approval: The study was approved by the institutional ethics committee*

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