"EFFECT OF PLATELET RICH PLASMA IN OSTEOARTHRITIS KNEE - A SHORT TERM FOLLOW UP"

By

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LIST OF ABBREVATIONS

YLD	Years Lived With Disability
IL	Interleukin
TNF	Tumour Necrosis Factor
IA	Intra Articular
HA	Hyaluronic Acid
PRP	Platelet-Rich Plasma
GF	Growth Factors
BMP	Bone Morphogenetic Proteins
TGF	Transforming Growth Factor
PDGF	Platelet Derived Growth Factor
MSC	Mesenchymal Stem Cells
OARSI	Osteoarthritis Research Society International
VEGF	Vascular Endothelial Growth Factor
VAS	Visual Analogue Scale
WOMAC	Western Ontario And Mcmaster Universities Osteoarthritis Index
ACP	Autologous Conditioned Plasma
K-L	Kellgren Lawrence
OMERACT	Outcome Measures In Rheumatology
ACL	Anterior Cruciate Ligament
PCL	Posterior Cruciate Ligament
MCL	Medial Collateral Ligament
LCL	Lateral Collateral Ligament
QoL	Quality Of Life
KOA	Knee Osteo Arthritis
PG	Prostaglandins
LK	Leukotriens
FGF	Fibroblast Growth Factors
VEGF	Vascular Endothelial Growth Factor
NGF	Nerve Growth Factor

ECM	Extra Celllular Matrix
MMP	Matrix Metalloproteinase
HGF	Hepatocyte Growth Factor
EGF	Epidermal Growth Factor
NO	Nitrous Oxide
GAG	Glycosaminoglycan
IGF	Insulin-Like Growth Factor
COX	Cyclooxygenase
EULAR	European League Against Rheumatism
NSAIDS	Nonsteroidal Anti-Inflammatory Drugs Nonsteroidal Anti-Inflammatory Drugs
MKS	Megakaryocytes

ABSTRACT

"EFFECT OF PLATELET RICH PLASMA IN OSTEOARTHRITIS KNEE- A SHORT TERM FOLLOW UP"

BACKGROUND:

Osteoarthritis (OA) is a painful chronic degenerative joint disease characterised by structural changes of the whole joint, which includes loss of articular cartilage, along with development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity.As of now, there are less options available for patients with mild to moderate arthritis. Most of the approaches are palliative and address the symptoms rather than influencing the biochemical environment of the joint or the disease process.By delivering very high concentrations of cytokines & growth factors (GF) to damaged tissues in the form of PRP, is considered to have a proven beneficial effect both on tendon and cartilage tissue regeneration. PRP is a newer treatment option emerging in the recent times and its efficacy needs to be examined in our population and hence the study.

OBJECTIVES:

To assess the functional outcome, reduction of pain and associated complications after intra articular injection of PRP in mild osteoarthritic knee joints.

MATERIALS AND METHODS:

It is a prospective, observational, time bound, hospital-based study conducted from November 2017 to May 2019, after obtaining institutional Ethical committee approval. 60 primary OA knee joints, included in this study, selected from R L Jalappa Hospital and Research centre, Department of Orthopaedics, Kolar. Patients of primary osteoarthritis of knee joints with Ahlbacks's

radiological grade I and II were included and Patients of secondary osteoarthritis of knee joints like post traumatic, inflammatory arthritis, Patients with active infections around knee joints and Platelet counts < 1 lakh were excluded. Autologous PRP prepared and infiltration was done under strict aseptic conditions. Patients assessed with WOMAC scoring &VAS for pain, before giving the PRP injection & after giving the injection at periods of 1 month, 3 & 6 months. The decrease in WOMAC & VAS scores was suggestive of improvement in patient's condition.

RESULTS:

Significant difference was observed in mean VAS and WOMAC total scores. The mean VAS score in Grade I reduced from baseline (6.78±0.67) to final follow-up (2.17±0.89) compared to Grade II which reduced from baseline (7.27±0.80) to final follow-up 3.16±1.26 with significant change in P value. The mean WOMAC TOTAL score in Grade I reduced from baseline (62.35±4.68) to final follow-up (14.22±4.26) compared to Grade II which reduced from baseline (68.59±8.16) to final follow-up (23.51±13.38) with significant change in P value.As we have given a working classification to assess the results, 6 (10%) joints have shown excellent results, 29(48.3%) joints have shown good results, 18(30%) joints have shown fair results and 7(11.7%) joints have shown poor results, among excellent results 5(27%) were Grade I and one (2.7%) Patient Grade II. No local or systemic complications noted during the study period.

KEY WORDS:

Osteoarthritis, Plate let rich plasma (PRP), Ahlbacks's, WOMAC, VAS.

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INTRODUCTION

Osteoarthritis (OA) is a painful chronic degenerative joint disease characterised by structural changes of the whole joint, which includes loss of articular cartilage, along with development of osteophytes, synovial inflammation, subchondral bone changes, meniscal damage, muscle weakness, and ligamentous laxity. OA is as a result of complex interplay involving genetic, metabolic, biomechanical, and biochemical factors.[1]

It is very common and debilitating disease, associated with a large social and economic burden.[2] Osteoarthritis of the knee joint is the fourth leading cause of 'years lived with disability' (YLD) and accounts for 3 % of total global YLD's.[3]

Current theories state that the disease progression is as a result of imbalance between pro inflammatory cytokines (including interleukin IL-1a, IL-β, and tumour necrosis factor-α & anti-inflammatory cytokines (including IL-4, IL-10, & IL-1ra). The resultant cytokine imbalance is believed to activate the proteolytic enzymes, leading to destruction of articular cartilage.[4]

As of now, there are less options available for patients with mild to moderate arthritis. Most of the approaches are palliative and address the symptoms rather than influencing the biochemical environment of the joint or the disease process.[5] Current pharmacotherapy of OA, such as analgesics, non-steroid and steroid anti-inflammatory drugs, glucosamine, chondroitin sulphate, and hyaluronic acid (HA), are predominantly directed toward the symptomatic relief of pain and inflammation, but they do little to reduce joint cartilage degeneration.[6]

Platelet-rich plasma (PRP) is defined as the autologous concentration of human platelets in a small volume of plasma, where platelet concentration is higher

(typically up to five times higher) than the normal platelet concentration.[7]PRP also includes concentration of several fundamental protein growth factors (GF) proved to be actively secreted by platelets to initiate mesenchymal tissue healing. These growth factors not only stimulate cell proliferation, differentiation, migration but also helps in matrix synthesis along with chondrocyte metabolism, chondrogenesis and improve cartilage healing in vivo.[8]

By delivering very high concentrations of cytokines & growth factors (GF) to damaged tissues in the form of PRP, is considered to have a proven beneficial effect both on tendon and cartilage tissue regeneration.[9] In OA involving knee joint, the main aim of PRP is not only to promote cartilage repair and relieve osteoarthritic symptoms but also in potentially delaying the need for joint replacement surgery.[10]

In view of these grey areas regarding our understanding and knowledge, this study is being designed to evaluate, the role & efficacy of PRP in early stages of knee osteoarthritis.PRP is a newer treatment option emerging in the recent times and its efficacy needs to be examined in our population and hence the study.

OBJECTIVES OF THE STUDY

- To assess the functional outcome and reduction of pain after Intra articular injection of PRP in mild osteoarthritic knee joints.

- To assess the complications associated with PRP infiltration in the osteoarthritis knee joints.

REVIEW OF LITERATURE

Marx et al. in the year 1998 first time used PRP in bone repair who studied on 88 patients having mandibular defects, were treated with bone grafting. In half of these patients PRP was also added to the bone graft and have shown an increase in maturity and consolidation of graft in subsequent radiographs.[11]

Anitua et al. in 2004 had stated that platelets release multiple growth factors having a chemotactic and mitogenic effect on mesenchymal stem cells and osteoblasts and therefore accelerate bone healing.[12]

Lucarelli et al. in 2005 estimated the efficacy of PRP on proliferation of human stem cells and observed that there are markedly increased cell numbers with an increase in concentration of PRP from 1% to 10%.[13]

Pietrzak and Eppley around the same time concluded from their study, that PRP set the pace of wound healing by the placement of a supraphysiological concentration of autologous platelets at the site of tissue injury.[14]

Tomoyasu et al. in 2007, by their study found that PRP and its soluble fraction stimulated osteoblastic differentiation of myoblasts and osteoblastic cells in the presence of BMP-2, BMP-4, BMP-6 and BMP-7, suggesting that platelets contain not only the growth factors for proliferation but also novel potentiators.[15]

Kajikawa et al. in 2008 had described, the role of PRP in activating circulation derived cells toward an injection site. It was postulated that PRP can both inhibit excess inflammation and also augment stem cell proliferation and maturation, as demonstrated in, invitro studies.[16]

In the same study authors speculated a possible role for PRP in tendon healing. Growth factors like TGF-b and PDGF have potent effects on cell proliferation, matrix synthesis, and chemotaxis.[16]

Sampson et al. in 2010 treated a small set of patients affected by primary and secondary OA knee and reported a favourable outcome in almost all the patients and that those who benefited from the injection series maintained those positive results for at least twelve months.[5]

A study done by Sanchez et al. in 2012 supported the safety, tolerability and efficacy of 'PRP' injections for both relief of pain and improved functional outcome in a limited patient having OA of the hip.[17]

A study done by Y Zhu et al. in 2013 stated that PRP is promising for treating injuries of cartilage. PRP has shown, anabolic effect on both chondrocytes and bone-marrow derived stem cells with resulting increases in proliferation of cells and production of matrix & anti-inflammatory effect via catabolic signalling pathways downregulation. Maybe it is a feasible, economic, and secure way to induce Mesenchymal stem cells (MSC) differentiation into chondrocytes integrally and expand cartilage cells in vitro.[18]

Patel et al. in 2013 based on their study concluded that short-term effectiveness of PRP injection compared with placebo for relieving pain and joint stiffness and improving knee functions in early osteoarthritis. There are more benefits in early OA, and according to author's experience, the effective of single dose of PRP is same as a double dose.[19]

A prospective study done by Filardo et al. in 2013 concluded that PRP injections can reduce pain and improve knee functional status at short term follow-up. Patients having a lower degree of joint degeneration are the better responders, whereas in severe osteoarthritic knees this biological treatment, used as a "salvage procedure", produced a less favourable outcome.[20]

A prospective, randomized study by Gobbi et al.in 2014 concluded that intra-articular PRP injection for early stages of OA with symptoms, are a valid treatment option. Significant pain reduction and improvement in function after 12 months was noted. Even though the beneficial effects are ill sustained after 2 years, the results are encouraging when compared to the pre-treatment function.[21]

Hassan et al.in 2014 concluded in their study that this treatment method is very safe and no complications such as infection or fever observed among patients. Mild pain at injected area and skin bruises detected.[22]

Osterman et al. in their study at Connecticut, U.S.A in 2015 assessed 2 different PRP preparations and their anti-inflammatory effects over time on human OA cartilage and synovium. Both had a significant anti-inflammatory effect on expression of gene but there is no difference in the anti-inflammatory effect between the 2 preparations.[23]

Almasry et al.in 2015 observed from their study that intra articular PRP injection could produce optimizing effects in surgically induced OA in the form of; decreasing the OARSI score, improving the inflammatory events in synovium and modulating the PDGF‐A and VEGF serum levels and synovial tissue immunoexpression. These effects could be reflected positively on the associated chondral defect.[24]

A review of overlapping meta-analyses by K. A. Campbell et al.in 2015 in U.S.A stated that Intra articular-PRP injection is a viable treatment for osteoarthritis knee & this method has the potential to produce symptomatic relief. Increased risk of local adverse reactions after multiple PRP injections observed. This method offers better symptomatic pain relief for the patients having early degenerative changes in knee and use of this method should be considered in patients with Knee OA.[25]

A one year randomized clinical trial by Raeissadat et al. in 2015 at Iran. Suggested that PRP injection is more efficacious than HA injection in improving quality of life & also reducing symptoms. It is a therapeutic option in knee osteoarthritic patients who have not responded to conventional treatment.[26]

In the year 2015, Calis et al. concluded that WOMAC & VAS scores were improved by the end of sixth month, and a significant increase in knee cartilage thickness measured by ultrasonography.[27]

Forogh et al. in 2016 demonstrated that single injection of PRP decreased joint pain more and short-term enhancement of activity of daily living along with quality of life in comparison with corticosteroids.[28]

Smith et al.in the same year, came to a consensus that no adverse reactions reported for ACP administration. After 1 year, WOMAC scores for the ACP subjects had improved by 78% from their baseline score, whereas scores for the placebo control group had improved by only 7%. Other joints affected with OA may also benefit from this treatment.[29]

Martini et al. in 2017 found that one dose of PRP in patients with OA knee with grade I or II, is very safe & effective treatment in managing the symptoms associated with this pathology, especially pain, and improving quality of life of patients.[30]

Fawzy etkal. in 2017 reduction in specific OA biomarker Serum collagen 2-1 following intra-articular PRP injection emphasize that PRP could be a promising safe and tolerable effective therapeutic option which improves function from basal states in primary knee OA patients.[31]

Kanwat et al. around the same time observed that intra-articular PRP injection results in reduction of synovial inflammation and vascularity as compared to controls,

which may be the biological basis of improvement in pain after PRP injection along with short term chondro-protective effect.[32]

Shen et al.also in the same year concluded that intra-articular PRP injections probably are more efficacious and safer in managing OA knee, in terms of pain relief and self-reported function improvement at 3, 6, and 12 months follow-up, compared with other injections, including saline placebo, HA, ozone, and corticosteroids.[33]

Deepak et al. in 2018 concluded in their randomised control study that PRP injection in Grade I & Grade II (Ahlback's radiological grading) does give pain relief and improves knee stiffness and functionality without any major adverse effects so this can be recommended as a viable modality of treatment.[34]

From the same series, authors also opined about the duration of the effect, which reduces early in patients who continue to pursue heavy works compared to those with sedentary lifestyle. But there was no significant difference between single versus double injection protocol, and they concluded that double dose doesn't offer any additional advantage.[34]

Sucuoğlu et al.in 2019 concluded that PRP injections provided a meaningful improvement of even chronic pain for patients with knee OA throughout a 12-week period. The pain reduction response to PRP was found to be significant in patients having early-stage knee OA.[35]

Southworth et al. in 2019 concluded that PRP found to be most beneficial for early kellegren lawrance (K-L) grade OA compared with more advanced OA. Better outcomes are seen with younger individuals with cartilage defects or earlier OA, and worse outcomes tend to be seen in patients above 50 years of age and those with further degenerated joints.[36]

A study by O'Donnell et al. in the same year noticed, age of the patient and OA disease state influence PRP bioactivity and suggested PRP prepared from older patients with OA may lower chondrocyte matrix synthesis and promote the inflammatory macrophage phenotype.[37]

Guillibert et al. also around the same time of the year observed that administration of single high volume of autologous pure PRP provided significant clinical benefit to more than 80% of responders at three months according to OMERACT-OARSI definition, in patients with knee OA in stage II or III according Kellgren–Lawrence scale.[38]

RELEVANT ANATOMY

Knee joint is the largest and most complicated joint in the body. It consists of two condylar joints between the medial and lateral condyles of the femur and the corresponding condyles of the tibia, and a gliding joint, between the patella and the patellar surface of the femur.[39]

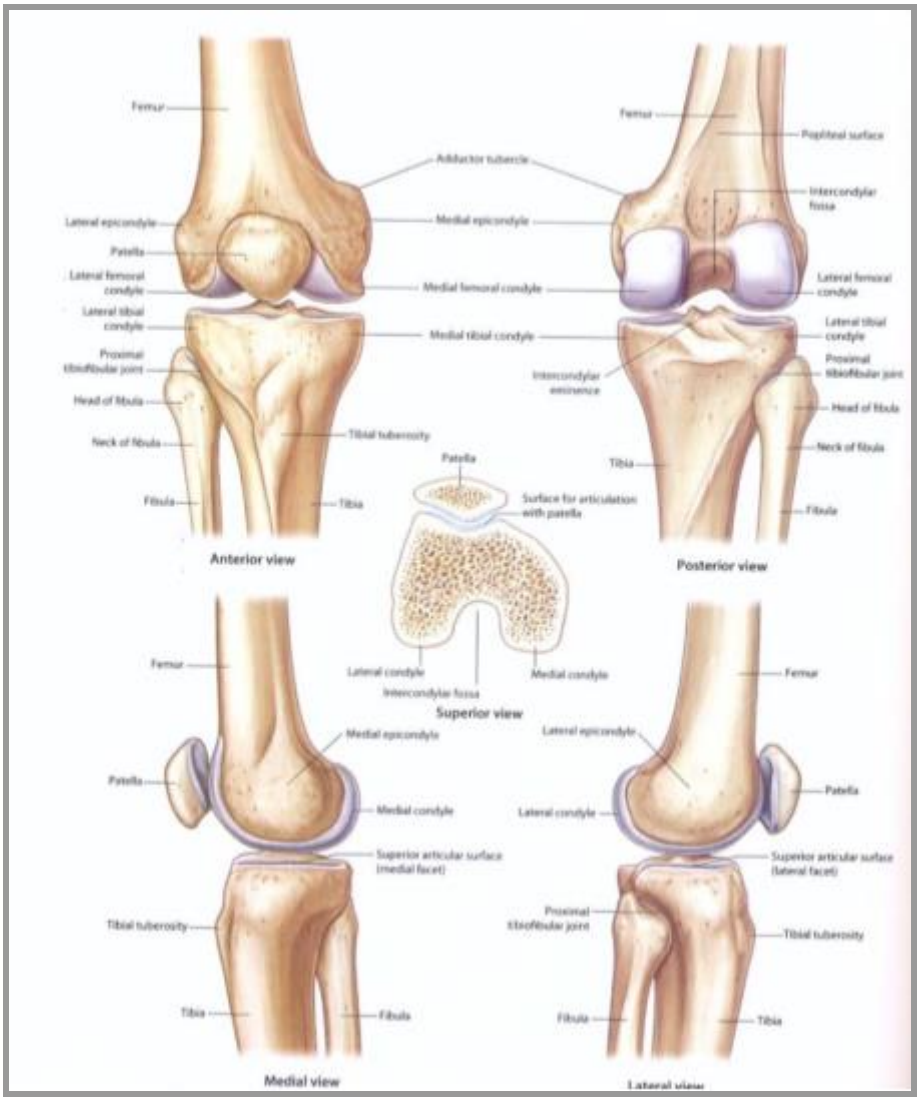


Figure 1: Bones forming knee joint.[39]

TYPE: -

The joint between the femur and tibia is a synovial joint of the hinge variety, but some degree of rotatory movement is possible. The joint between the patella and femur is a synovial joint of the plane gliding variety.

ARTICULATIONS: -

Proximally are rounded condyles of the femur, distally are the condyles of the tibia and their cartilaginous menisci, in front is the articulation between the lower end of the femur and patella.

The articular surfaces of the femur, tibia, and patella are covered with hyaline cartilage. The articular surfaces involving, medial and lateral condyles of tibia are often referred as medial and lateral tibial plateaus.

CAPSULE: -

The capsule is attached to the articular surface margins and surrounds the side and posterior aspects of the joint. In the front of joint, the capsule is absent, permitting the synovial membrane to pouch upward beneath the quadriceps tendon, forming the suprapatellar bursa. On each side of the patella, the capsule is strengthened by expansions from the tendons of vastus lateralis and medialis. Behind the joint, the capsule is strengthened by an expansion of the semimembranous muscle called the oblique popliteal ligament. An opening in the capsule behind the lateral tibial condyle permits the popliteus tendon to emerge.[39]

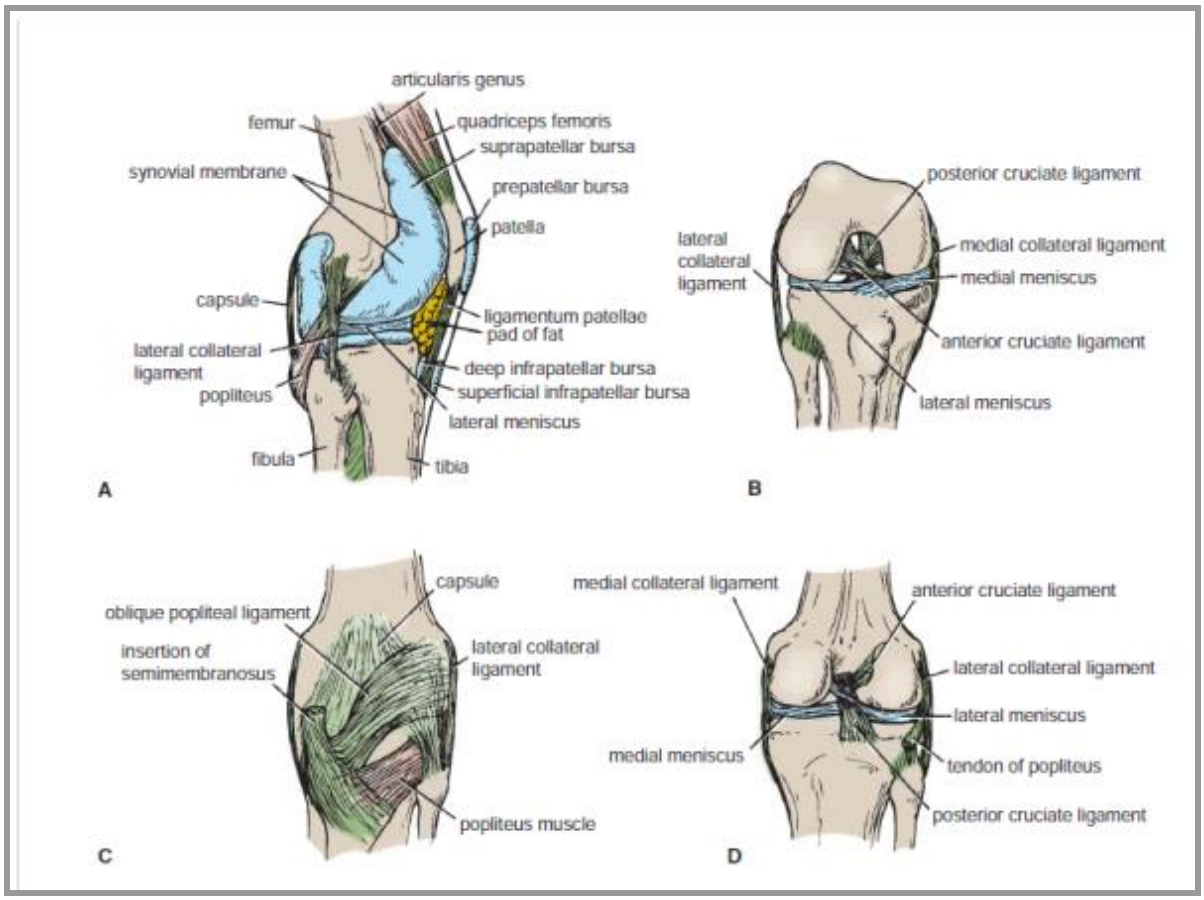


Figure 2: A. The right knee joint as seen from the lateral aspect. B. The anterior aspect, with the joint flexed. C, D. The posterior aspect.[40]

LIGAMENTS: -

The ligaments may be divided into extracapsular (Those that lie outside the capsule), and intracapsular (Those that lie within the capsule).

A. Extracapsular Ligaments: -

The ligamentum patellae is attached above to the lower border of the patella and below to the tuberosity of the tibia.

The lateral collateral ligament (LCL): Cordlike and is attached proximally to the lateral condyle of the femur and distally to head of fibula.

Medial collateral ligament (MCL): Flat band and attaches proximally to the medial condyle of the femur and distally to the medial surface of the shaft of the tibia. It is tightly attached to the edge of medial meniscus.

Oblique popliteal ligament: Tendinous expansion derived from the semimembranosus muscle and also helps in strengthening the posterior aspect of the capsule.

B. Intracapsular Ligaments: -

The cruciate ligaments are two strong intracapsular ligaments that cross each other inside the joint cavity.

The ACL is attached to the anterior intercondylar area of tibia and passes upward, backward, and laterally and attached to the posteriorly to the medial surface of lateral femoral condyle.

The PCL is attached to posterior intercondylar area of tibia and passes upward, forward, and medially attached to anterior part of lateral surface of medial femoral condyle.[41]

MENISCI: -

The menisci are C-shaped sheets of fibrocartilage. The peripheral border is thick and attached to capsule, and the inner border is thin and concave and forms a free edge. The upper surfaces & lower surfaces are in contact with femoral condyles tibial condyles respectively.[42]

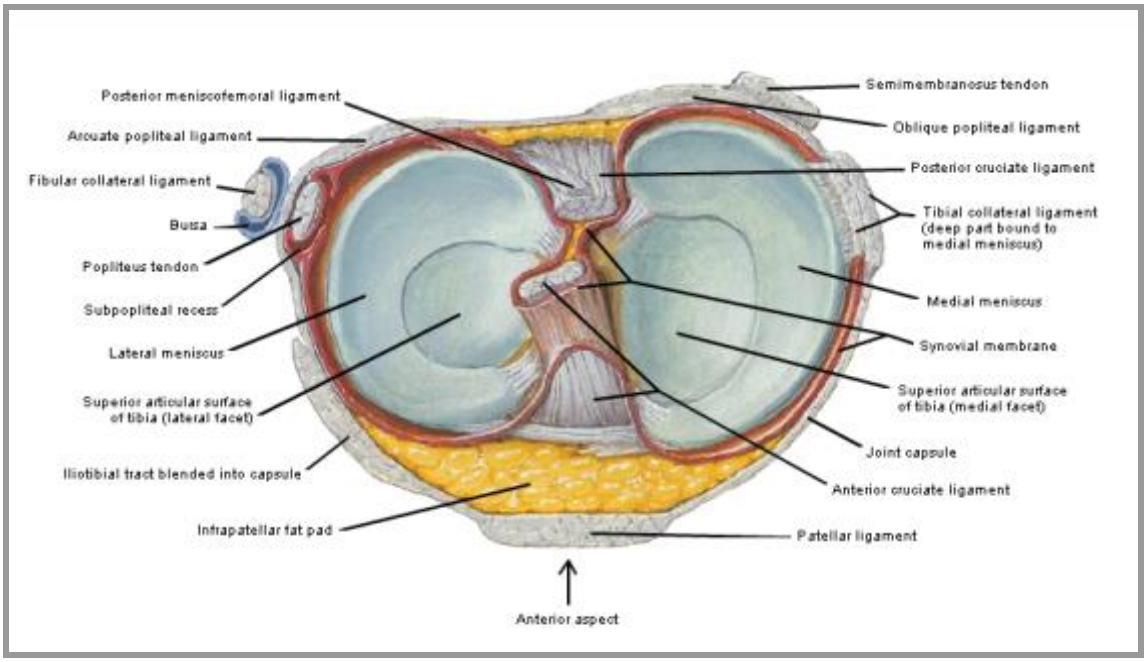


Figure 3**:** Superior view of the knee joint.[43]

SYNOVIAL MEMBRANE: -

The synovial membrane lines the capsule and attached to articular surfaces margins. Infront and above the joint, it forms a pouch, which extends up beneath the quadriceps femoris muscle for three fingerbreadths above the patella, forming the suprapatellar bursa.

At the back of the joint, the synovial membrane is prolonged downward on the deep surface of tendon of the popliteus, forming the popliteal bursa.The synovial membrane is reflected forward from the posterior part of the capsule around the front of cruciate ligaments. As a result, the cruciate ligaments lie behind the synovial cavity and are not bathed in synovial fluid.[42]

BURSAE AROUND THE KNEE JOINT

1. Anterior Bursae: -
    - The suprapatellar bursa
    - The prepatellar bursa
    - The superficial infrapatellar bursa
    - The deep infrapatellar bursa
2. Posterior Bursae: -
    - The popliteal bursa
    - The semimembranosus bursa
3. The remaining four bursae are found related to
    - The tendon of insertion of the biceps femoris;
    - Related to the tendons of the sartorius, gracilis, and semitendinosus muscles;
    - Beneath the lateral head of origin of the gastrocnemius muscle; and
    - Beneath the medial head of origin of the gastrocnemius muscle.[42]

NERVE SUPPLY: -

The femoral, obturator, common peroneal, and tibial nerves supply to the knee joint.

MOVEMENTS: -

Knee joint can perform flexion, extension, and rotation. As knee joint assumes the position of full extension, medial rotation of the femur results in a twisting & tightening of all major ligaments of the joint, and the knee joint becomes a mechanically rigid structure; the cartilaginous menisci are compressed like rubber cushions between the femoral and tibial condyles. The extended knee is said to be in the locked position.[43]

Table 1: Muscles producing movements at the knee joint.[43]

Movement	*Principal muscles*
A. Extension (from sitting on a chair to standing)	Quadriceps femoris (four heads)
B. Locking (standing in "attention")	Vastus medialis
C. Unlocking (standing "at ease")	Popliteus
D. Flexion	1. Biceps femoris 2. Semitendinosus 3. Semimembranosus
E. Medial rotation of flexed leg	1. Popliteus 2. Semimembranosus 3. Semitendinosus
F. Lateral rotation of flexed leg	Biceps femoris

ARTICULAR CARTILAGE[44]

Hyaline (literally, ‘glass-like’) cartilage coats the articular surfaces of synovial joints. It is composed of individual chondrocytes bound together by an extracellular matrix.

It is avascular, aneural, alymphatic and almost nonimmunogenic. It is nourished entirely via diffusion from the synovial fluid.

Components of the extracellular matrix are

a. Water (75 per cent wet weight of articular cartilage),
b. Proteoglycans (10–15 per cent wet weight).
c. Type II Collagen fibres (almost exclusively type II) constitute around 10–20 per cent wet weight (40–70 per cent dry weight), forming a meshwork with high tensile strength.
d. Chondrocytes (5 per cent wet weight) manufacture and maintain the extracellular matrix.

STRUCTURE OF ARTICULAR CARTILAGE

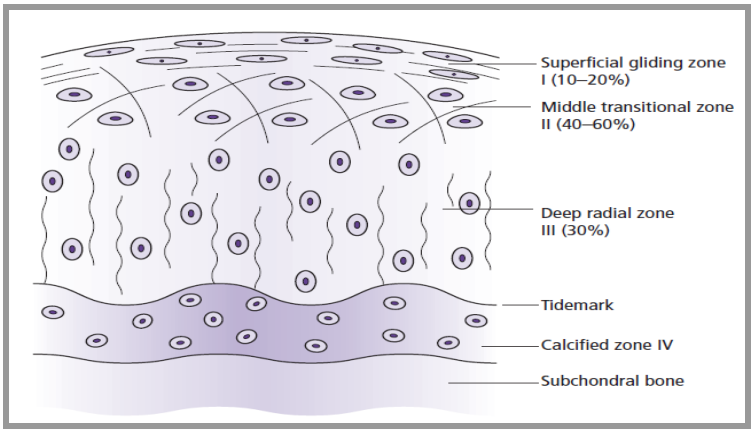


Figure 4: Articular cartilage layers seen on histological section[44].

FUNTIONS OF ARTICULAR CARTILAGE

The function of hyaline cartilage is to distribute weight-bearing forces and joint lubrication (allowing movement between opposing surfaces with the minimum of friction and wear) and shock absorption (distributing joint loads and therefore reducing the stresses experienced).[44]

CHANGES IN OSTEOARTHRITIC CARTILAGE

Table 2: Biochemical changes seen with ageing and osteoarthritis in cartilage.[45]

	Ageing	Osteoarthritis
Water content	*Decreases*	*Increases (90% compared with normally 65–80%)*
Synthetic activity	*Decreases*	*Increases*
Collagen	*Unchanged*	*Breakdown of matrix framework leads to decrease in collagen, but relative concentration increases due to loss of PGs*
PG content	*Decreases (length of protein core and GAG chains decreases)*	*Decreases*
PG synthesis	*Decreases*	*Increases*
PG degradation	*Decreases*	*Increases very significantly*
Chondroitin sulphate (both 4- and 6-)	*Decreases*	*Increases*
Keratan sulphate	*Increases*	*Decreases*
Chondrocyte size	*Increases*	
Chondrocyte number	*Decreases*	
Modulus of elasticity	*Increases*	*Decreases due to increased water content; increased water content also causes increased permeability and decreased strength*
Enzymes		*Increased activity of MMPs*
Matrix subunit molecules		*Increased levels, e.g. COMP, aggrecan (in synovial fluid and serum)*

COMP, cartilage oligomeric protein; GAG, glycosaminoglycans; MMP, matrix metalloproteinase; PG, proteoglycan.

OSTEOARTHRITIS OF KNEE

Osteoarthritis (OA) is a chronic degenerative disease of the joint resulting from the degradation of articular cartilage, degradation and proliferative reformation of subchondral bone & a low degree of synovitis that leads to a reduced quality of life (QoL).[46]

Osteoarthritis is a chronic arthropathy, which is characterized by debilitating pain and consequent hampering of day-to-day activity, most commonly affecting the knee and the hip joints.[32] Due to the high use and stress, knee joint is a frequent site for painful conditions including OA.[47]

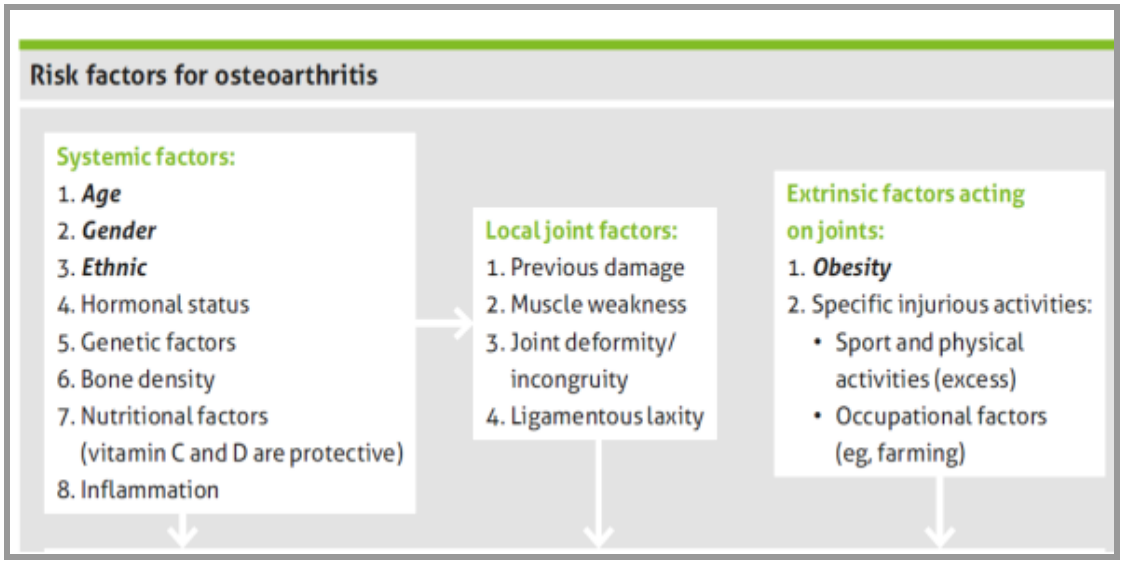
Osteoarthritis is the most frequent joint disease with a prevalence range of about 22% to 39% in our country. OA is more commonly seen in women than in men, but the prevalence increases dramatically with the age. Nearly, about 45% of women > 65 years age have symptoms, while radiological evidence can be found in 70% of those > 65 years.[48]

Osteoarthritis knee is one of the leading causes of mobility impairment, particularly among females & is estimated as 10th leading cause of nonfatal burden.[48] Osteoarthritis knee is found to have, high prevalence rate compared with other sites of OA. The incidence increases with age & with longer lifetime and higher average weight of the population, particularly in obese women.[49]

Knee Osteoarthritis is one of the major causes of lower extremity disability in elderly adults, especially people older than 45 years. Besides causing local pain, stiffness & swelling, it is one of the common causes of low back pain and decreased quality of life.[50]

The aetiology of knee OA is multifactorial and still completely not understood. Age, obesity, lower-limb malalignment, defects of cartilage, joint instability, previous fractures, and meniscectomy surgery are strongly correlated to knee OA.[30]

Table 3: Risk factors for osteoarthritis.[51]



The osteoarthritis development is dependent to interactions between several factors and so this process may be considered the product of an interplay between systemic and local factors.[52]The pathophysiology of knee OA is complex; inflammatory cytokines and proteolytic molecules have been implicated and represent the primary substances contributing to this disease.[53]

In osteoarthritis, the synovial fluid contain multiple inflammatory mediators including plasma proteins (C-reactive protein, proposed as marker in development and also in progression of OA), prostaglandins (PGE2), leukotrienes (LKB4), cytokines (TNF, IL1β, IL6, IL15, IL17, IL18, IL21), growth factors (TGFβ, FGFs, VEGF, NGF), nitric oxide, & complement components.[53,54]

In OA knees, chondrocyte senescence and loss of cartilage integrity are major features. Increase in water content of hyaline cartilage, accompanied by

corresponding decrease in proteoglycan concentration, length and aggregation, causing reduced cartilage stiffness and fibrillation of the cartilage surface. From this, cartilage proceeds to erode and deep clefts may form. Concurrently, morphological changes in subchondral bone are found. As synovial fluid infiltrates, the formation of subarticular cysts in the subchondral bone also occurs. Osteophytes (bony projections) are very characteristic of OA knee in non-pressure areas, because of flattening of bone from pressure in high-wear and tear areas.[46]

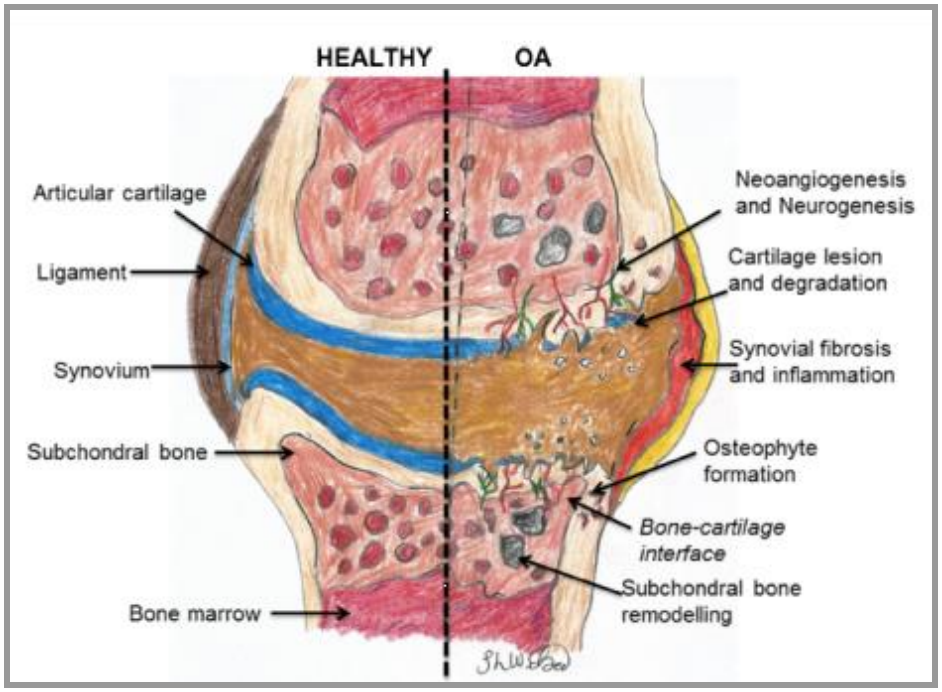


Figure 5: Comparison of a healthy (left) and OA knee joint (right).[46]

Although cartilage destruction is considered as hallmark of disease; synovitis, subchondral bone remodeling (thickening, bone collapse, bone cysts), degeneration of ligaments and menisci, & hypertrophy of joint capsule take parts in the pathogenesis of OA.[55]

The loss in articular cartilage, probably initiated as focal lesion, may progressively extend and produce changes in loading, thereby increasing loss of cartilage. This pathoanatomical description of cartilage loss process involves morphologic and metabolic changes in chondrocytes, biochemical and structural changes in the ECM, because of complex mechanical, biological, biochemical, molecular, and enzymatic feedback loops.[56]

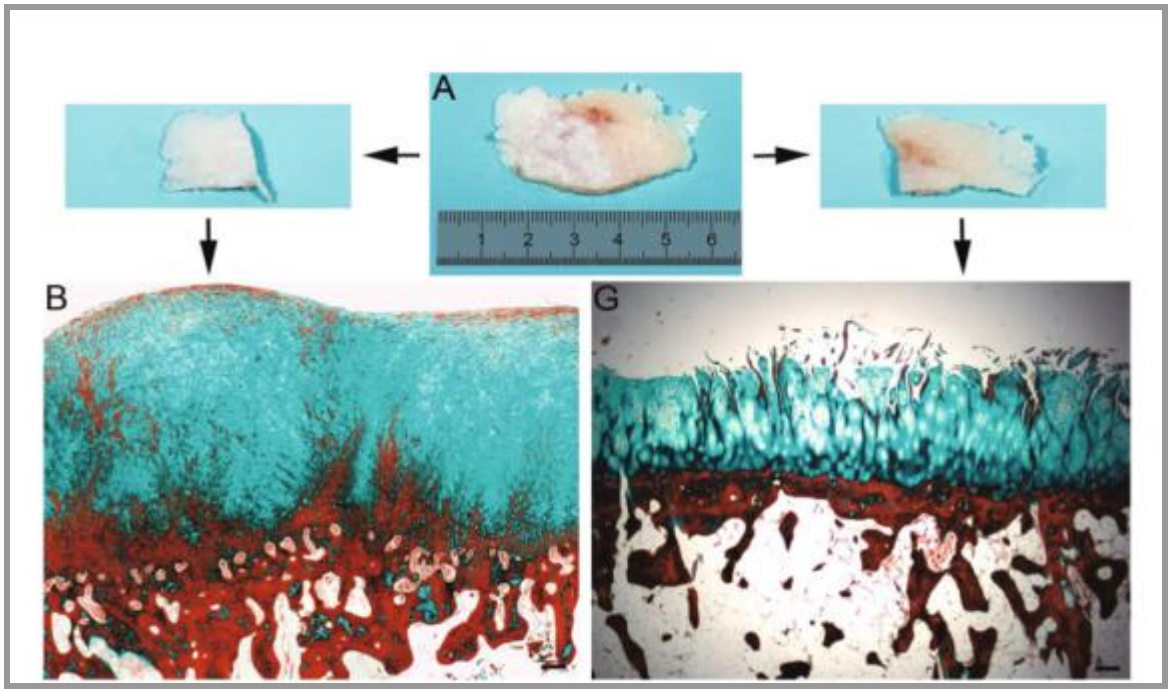


Figure 6: A) Macroscopic morphology of osteoarthric cartilage,

B) and G) show panoramic images of the sample (Masson's trichrome staining).

comparison of a healthy (left) and OA knee joint (right)[57].

METABOLIC AND BIOCHEMICAL CHANGES IN CARTILAGE OF OSTEOARTHRITIS:-

Generalized increased hydration and swelling with loss of tensile strength is noticed in early OA, whereas increase in type I collagen synthesis and progressive fall occurs in proteoglycan concentration in later stages of OA. Specific collagens – Initial swelling of collagen fibrillary network with loss of type II collagen, specific cleavage of collagens & loss of tensile strength with increased content of collagen type IV. Type III and X collagen are also synthesized. Proteoglycans show increased extractability and decrease in monomer size because of specific cleavages by aggrecanases and metalloproteinases. Cytokines, proteinases and inhibitors – There is increase in pro-inflammatory cytokines, aggrecanases, MMPs (matrix metallo roteinase), cathepsins and decrease in overall inhibitors.[58]

GROWTH FACTORS AND CYTOKINES

A) ANABOLIC GROWTH FACTORS

TGF (transforming growth factor beta- 1, 2 & 3) help in chondrocyte proliferation, matrix synthesis, modulate effects of IL-1 and increases proteinase inhibitors. Fibroblast and PDGF also help in differentiation and proliferation of chondrocytes and MMP production. Insulin growth factor-1 (IGF-1) increases glycosaminoglycan (GAG) & collagen synthesis. Bone morphogenetic proteins increase matrix synthesis. [58]

B) CATABOLIC FACTORS

Interleukin-1(IL-1) & tumor necrosis factor α increases MMPs, inhibit GAG synthesis & can further potentiate the degenerative cascade. Oncostatin-M combines with IL-1 and TNF to promote matrix breakdown. Others like IL-17 and IL-18 increase expression of IL-1 beta and IL-6 and increase MMP. NO (nitric oxide) can inhibit collagen and proteoglycan synthesis, NO is a major catabolic factor produced by chondrocytes, can activate MMPs causing an oxidative injury and produce apoptosis leading to degradation of articular cartilage. Prostaglandin effect on chondrocyte metabolism are complex and include enhanced type II collagen synthesis, activation of MMPs, and promotion of apoptosis. Moreover, COX-2 inhibition prevents IL-1beta induced proteoglycan degradation.[58]

C) REGULATORY FACTORS

Interleukin-6 increases proteinase inhibitors production and proliferation of chondrocytes while IL-4, IL-13 and interferons oppose effects of proinflammatory cytokines. IL-1 receptor antagonist blocks effect of IL-1**.**[58] Osteoarthrits is classified into 2 different groups based on its aetiology: primary (idiopathic or non-traumatic) and secondary (usually due to trauma or mechanical misalignment).[59] Persistent knee pain, limited morning stiffness, and reduced function are the three symptoms that are recommended by EULAR for diagnosing knee OA. Crepitus, joint movement restriction and bony enlargement are also very useful for the diagnosis of knee OA.[60] Knee joint pain is the most common symptom in knee OA, a leading cause of chronic disability, & a major source of the disability attributable to OA Pain, in knee OA typically exacerbates by activity and relieves by rest.[60]

A clinical diagnosis of knee OA is supported by, presence of typical symptoms, clinical examination findings, laboratory results, and imaging features. No single clinical feature is sensitive or specific. Generally, the more features that are present, the more likely the diagnosis.[16]

Table 4: Symptoms and signs of OA Knee.

SYMPTOMS	SIGNS
Persistent Knee Pain	Crepitus
Limited knee stiffness (<30 min)	Restricted Movements
Reduced function	Bony Enlargement

Diagnosis of knee OA can be made by both clinical findings & physical examination; however, identification of joint damages is necessary to confirm diagnosis and to know the extent of joint involvement.[60] Radiographic images of an arthritic knee may show narrowed joint space because of articular cartilage loss, changes in bone, and formation of bone spurs (osteophytes) caused by bone remodelling.[51]

Table 5: Radiographic features of osteoarthritis knee.

RADIOGRAPHIC FEATURES OF OSTEOARTHRITIS KNEE
➢ Osteophytes
➢ Joint space narrowing
➢ Subchondral sclerosis
➢ Sub chondral cyst

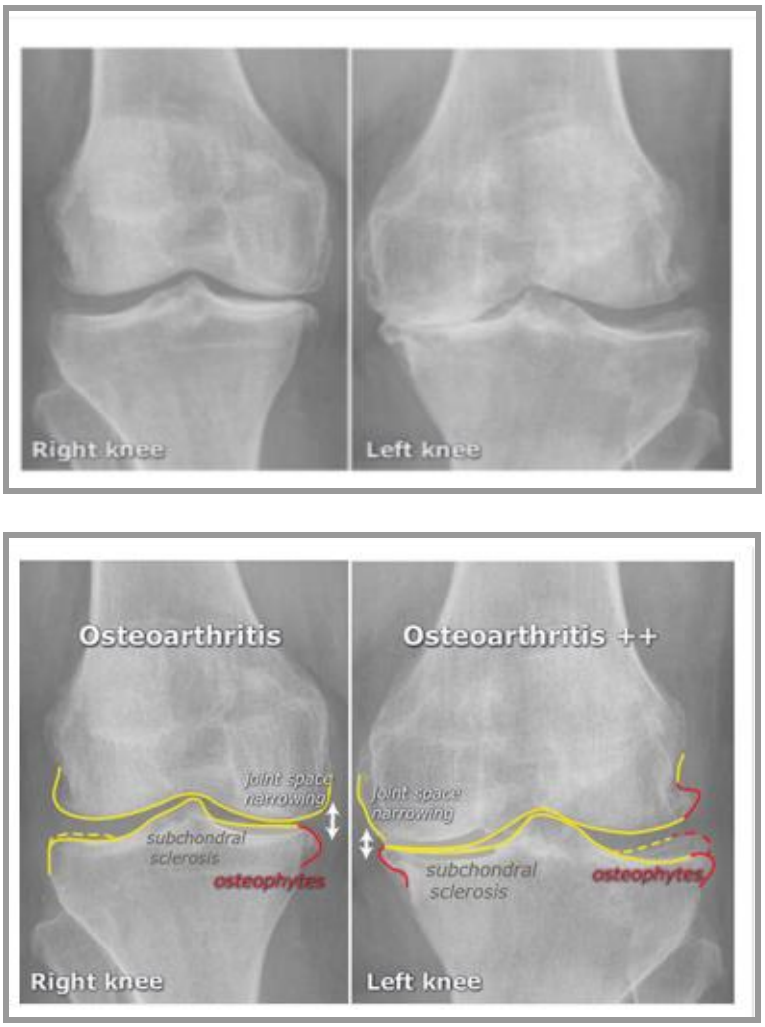


Figure 7: Radiographic features of osteoarthritis knee[51].

Radiography is currently the most widely used method that can classify the severity of knee OA is done using either the “Kellgren and Lawrence system or the Ahlbäck classification system”.[61]The “Ahlback classification”, published in 1968, it is probably the most quoted classification in the literature, and is still widely used in clinical practice.[62]

The targets of OA treatment are pain decrement, function and mobility increment, prevention or correction of the deformity, and slowing the progression of the disease. There are numerous conservative treatment methods for knee OA that have short-term efficacy and have their own benefits and disadvantages.[63]

Managing patients with early osteo arthritis of knee requires a combination of non-pharmacological and pharmacological treatments, including surgical interventions when necessary.[64] The current nonpharmacological treatments for symptomatic OA knee patients begin with patient education & self-management of his/her risk factors for OA, exercise, weight loss, physical therapy.[65]

Pharmacological options include topical anti-inflammatory gels; oral non-steroid anti-inflammatory drugs (NSAIDs); oral supplements, such as glucosamine and chondroitin sulphate; and injection therapies.[66] The four main injection therapies currently utilized are corticosteroids, hyaluronic acid (HA), platelet-rich plasma (PRP), and autologous mesenchymal stem cells (MSCs).[67]

Because of high costs of knee OA management, therapeutic options that are effective on tissue healing have been taken into consideration in recent years in order to prevent the progression of OA.[68]

PLATE-LET RICH PLASMA

Platelets are small anucleate cell fragments that have a characteristic discoid shape and range from 1 to 3 μm in diameter. Historically, platelets were referred to as cellular dust. Platelets are not only responsible for haemostasis, wound healing, inflammation, and innate immunity but also angiogenesis.[69] Platelets are formed from the cytoplasm of megakaryocytes (MKs), their precursor cells, which reside in the bone marrow.[69]

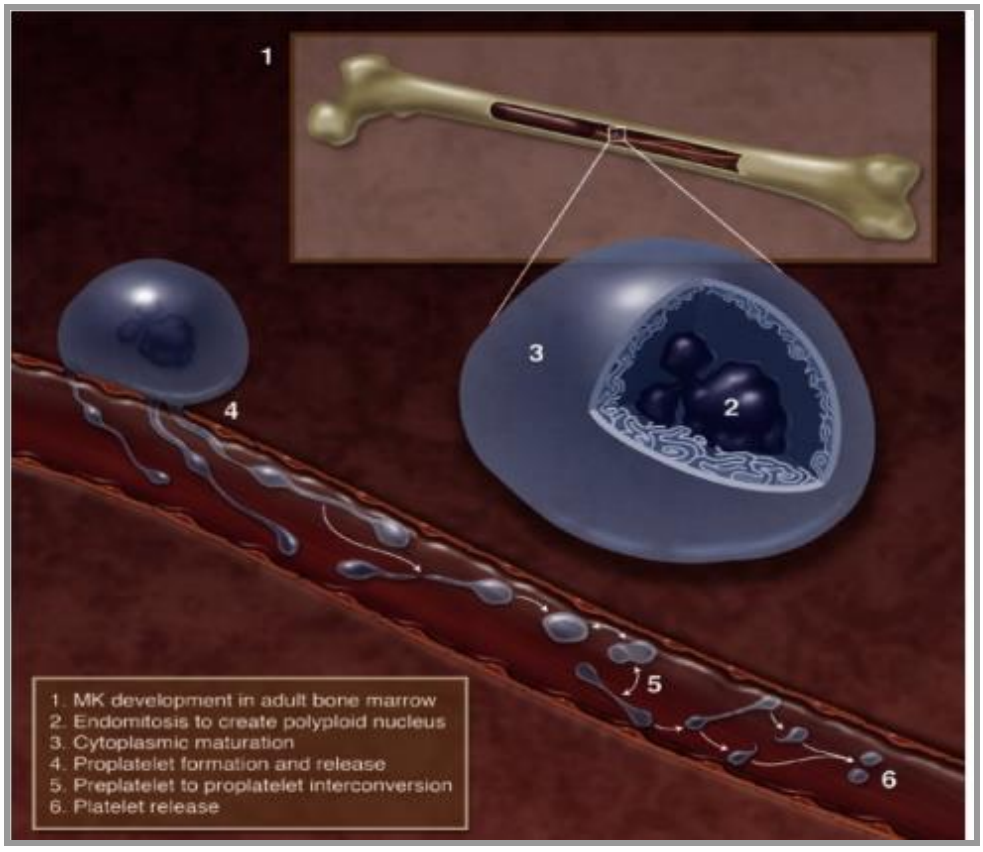


Figure 8: Formation of platelet from bone marrow[69].

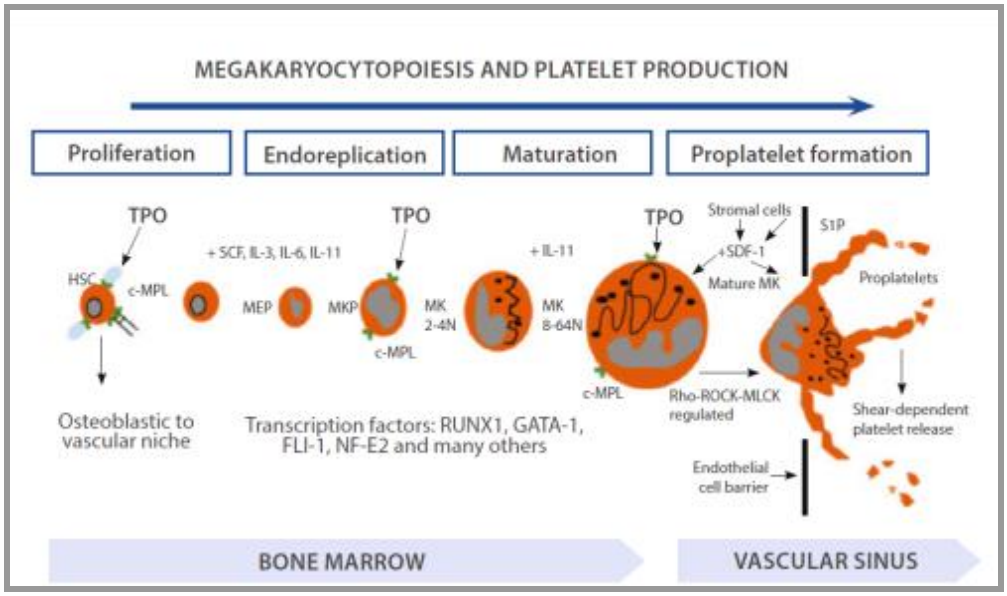


Figure 9: Schematic representation of megakaryocytopoiesis and platelet production.[70]

After they are shed from the cytoplasm of megakaryocytes, platelets circulate in the bloodstream for 9 to 11 days.[71]The two functional roles of platelets are haemostasis and the initiation of wound healing.[14]

The platelet cell membrane is trilaminar with a glycoprotein receptor surface overlying and partially interspersed with and penetrating a bilayer of phospholipids and cholesterol. They lack nuclei but contain organelles and structures such as mitochondria, microtubules, and granules (alpha, delta, and lambda).[14]

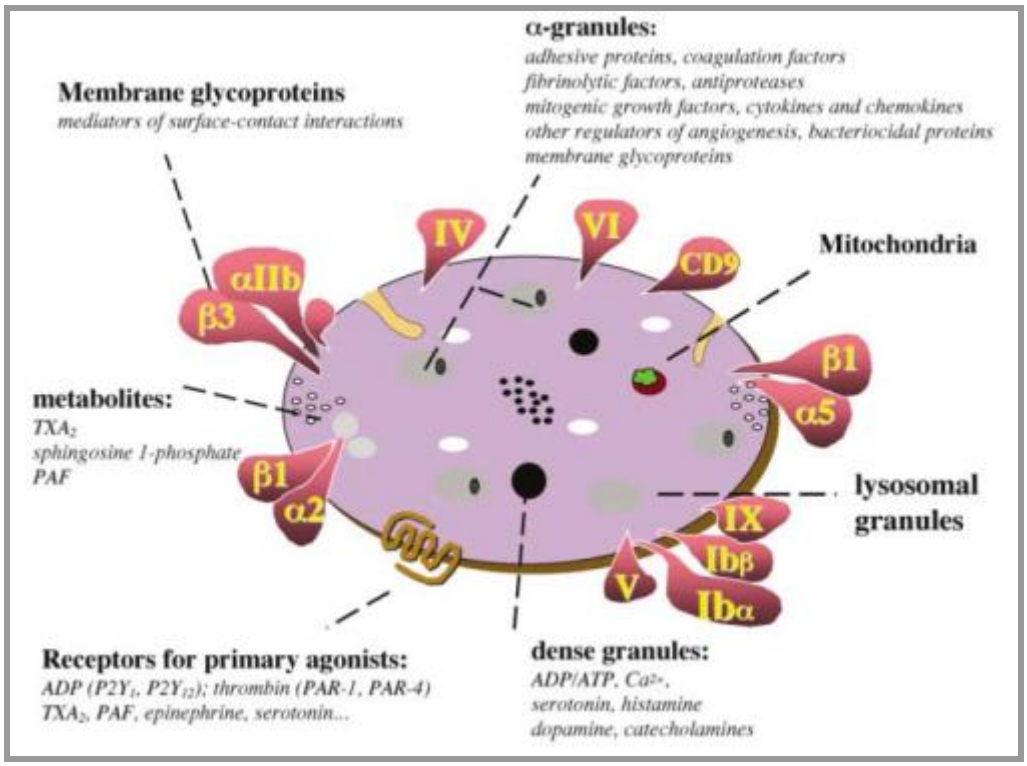


Figure 10: Structure of a Platelet.[72]

The alpha granules, bound by a unit membrane, are formed during megakaryocyte maturation, are about 200 to 500 nm in diameter, and number approximately 50 to 80 per formed platelet. They contain more than 30 bioactive proteins, many of which have a fundamental role in haemostasis or tissue healing.[73]

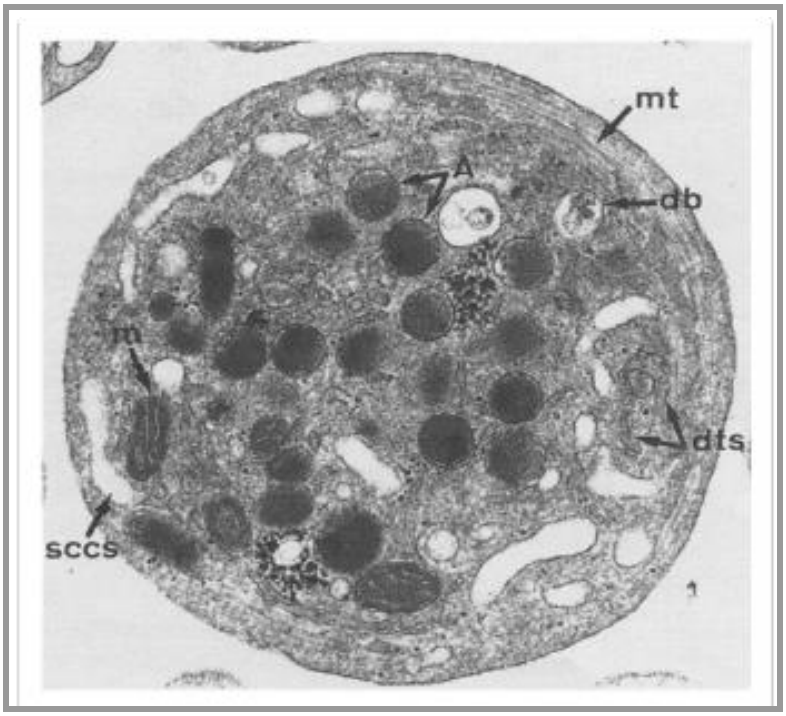


Figure 11: Platelet and its Granules[73].

Platelets to participate in tissue healing by secreting a variety of growth factors, cytokines, chemokines and other factors. For example, VEGF, platelet-derived growth factor (PDGFa/b and c), fibroblast growth factor (FGF), hepatocyte growth factor (HGF), epidermal growth factor (EGF), connective tissue growth factor (CTGF) & insulin-like growth factor (IGF).[74]

Table 6: Growth factors present in platelet-rich plasma[75].

Name	Acronym	Function
Platelet-derived growth factor	PDGF	Stimulates fibroblast production, chemotaxis, stimulates transforming growth factor–β1, collagen production, upregulation of proteoglycan synthesis
Transforming growth factor–β1	TGF-β1	Modulates proliferation of fibroblasts, formation of extracellular matrix, cell viability; increases production of collagen from fibroblasts, suppression interleukin 1–mediated effects on proteoglycan synthesis in cartilage
Basic fibroblastic growth factor	bFGF	Produces collagen; stimulates angiogenesis, proliferation of myoblasts
Vascular endothelial growth factor	VEGF	Promotes angiogenesis
Epidermal growth factor	EGF	Promotes cell differentiation, angiogenesis, proliferation of mesenchymal and epithelial cells

PRP is concentration of human platelets (autologous) in small volume of plasma, where the concentration of platelet is higher (typically up to five times higher) than the normal platelet concentration in a healthy person's blood.[73]

Evidence suggests that PRP has potential to have a regenerative effect on certain body tissues, added to the main role platelets play in haemostasis.[76]

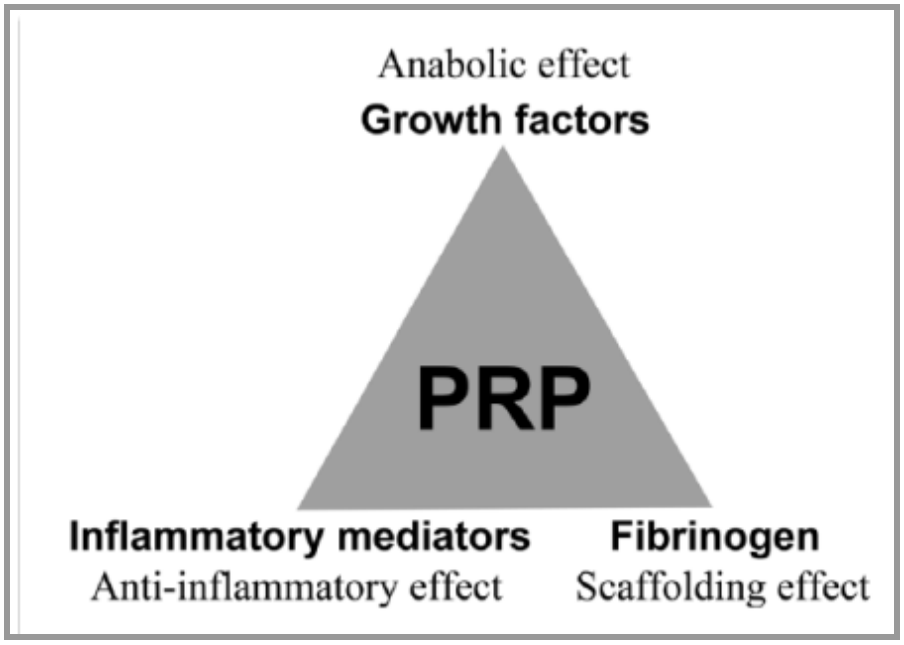


Figure 12: Principal components and potential effects and actions[77].

Platelet-rich plasma has gained increasing attention as a promising procedure to stimulate repair of the cartilage, because of growth factors (GFs) stored in platelet '**α** granules' which are found to play a role in regulation of articular cartilage.[68] Extracting PRP is easy and convenient, and processing is relatively simple and short, easy handling. It also offers multiple GFs at relatively inexpensive cost. Above all, its use is safe.[18]

It is a very minimally invasive method, to obtain a high concentrate of autologous GFs, which could be easily placed directly into the lesion site.[78] PRP is safe from immune reaction and blood diseases because it is obtained from autologous blood and also PRP can be administered in the outpatient clinic easily.[79] PRP therapy seems to delay operative approaches in early degenerative disease. In cases of advanced degenerative joint disease, operative approaches such as arthroscopy, osteotomy, and arthroplasty can be better treatments.[79]

MATERIAL AND METHODS

SOURCE OF DATA: -

It is a prospective, observational, time bound, hospital-based study conducted from November 2017 to May 2019, after obtaining institutional Ethical committee approval. 60 primary OA knee joints, included in this study, selected from R L Jalappa Hospital and Research centre, Department of Orthopaedics, Kolar, on outpatient and in-patient basis who meets inclusion criteria.

After clinical examination & radiographs of the knee joint in standing position (antero-posterior views and lateral views) were taken, Blood sample of the patient was collected and PRP prepared in Blood bank. Infiltration was done in Operation theatre under strict aseptic conditions.

Patients assessed with 'WOMAC" (Western Ontario McMaster Universities Arthritis Index) scoring & "VAS" (visual analogue scale) for pain, before giving the PRP injection & after giving the injection at periods of 1 month, 3 & 6 months. The decrease in WOMAC score & VAS score was suggestive of improvement in patient's condition.

INCLUSION CRITERIA

- Patients of primary osteoarthritis of knee joints with Ahlbacks's radiological grade I and II.

EXCLUSION CRITERIA

- Patients of secondary osteoarthritis of knee joints like post traumatic, inflammatory arthritis.
- Patients with active infections around knee joints.
- Platelet counts < 1 lakh.

AHLBACK RADIOLOGICAL GRADING OF OSTEOARTHRITIS OF KNEEJOINTS.[62]

- Grade 1– Joint Space narrowing (< 3mm)
- Grade 2 – Joint space obliteration
- Grade 3 – Minor bone attrition (0-5mm)
- Grade 4 – Moderate bone attrition (5-10mm)
- Grade 5 – Severe bone attrition (>10mm).

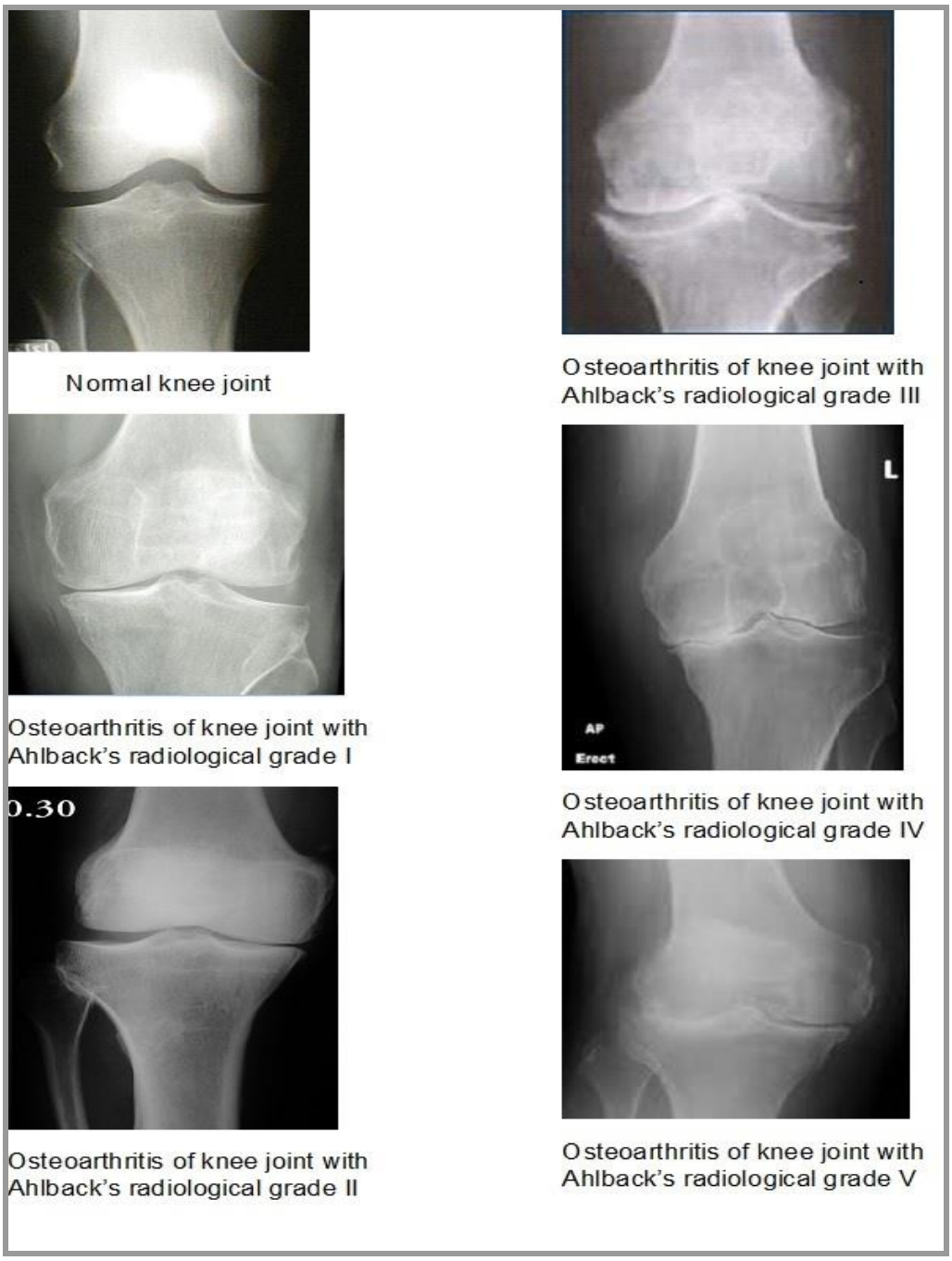


Figure 13: Ahlback's radiological grading of Osteoarthritis of knee joints.[62]

SAMPLE SIZE ESTIMATION

Sample size included in this study is calculated based on difference in mean VAS score (pre &post injection) in a study done by Patel et al. in the year 2013. observed any average variance estimate of 1.078 with 99% confidence interval with 80% power to detect difference of 10% reduction in pain score in estimated using paired T test.

$$t = \frac{\frac{\Sigma d}{N}}{\sqrt{\frac{\Sigma d^2 - \frac{(\Sigma d)^2}{N}}{N(N-1)}}}$$

d = difference between matched scores

N = number of *pairs* of scores

A ‘p’ value p=0.05 is considered as statistically significant

PATIENT SELECTION

All patients with primary knee osteoarthritis were evaluated clinically & radiographically. All the Patients with grade I and II Ahlback's radiological grading were included in the study, irrespective of age, sex & socioeconomic status.

Informed & written consent was obtained from patients participated in this study. Selected patient's blood sample was sent for CBC, random blood sugar. Blood sample was evaluated to assess the WBC & platelet count prior to the infiltration.

Patients having platelet counts < 100000/cubic mm, excluded from the study. Patients were also asked about intake of any oral medications like NSAIDS, if anyone is on any analgesics, they were instructed to stop one week before administration of PRP. For the selected patients 'WOMAC' score and 'VAS' score were recorded in a chart for each patient & follow up scorings were also noted down similarly in the same chart of that patient.

PREPARATION OF PLATELET RICH PLASMA (PRP)

After selecting patient fifty (50) ml of venous blood was collected from the antecubital vein atraumatically to avoid irritation & injury to the platelets by using a syringe. Blood was then transferred to vacutainers containing CPD-A1 (citrate phosphate dextrose and adenine) as anticoagulant. The vacutainers were centrifuged for a duration of 15 minutes at 1500 rpm in a table-top centrifuge with blood being separated into residual red blood cells & PRP. PRP was extracted through a pipette and then transferred to a sterile test tube.

The platelet count was assessed in final PRP extract & was used for injection with a 10-mL syringe. The mean platelet count achieved in this method by us was higher than 5 times the normal platelet count of that patient.

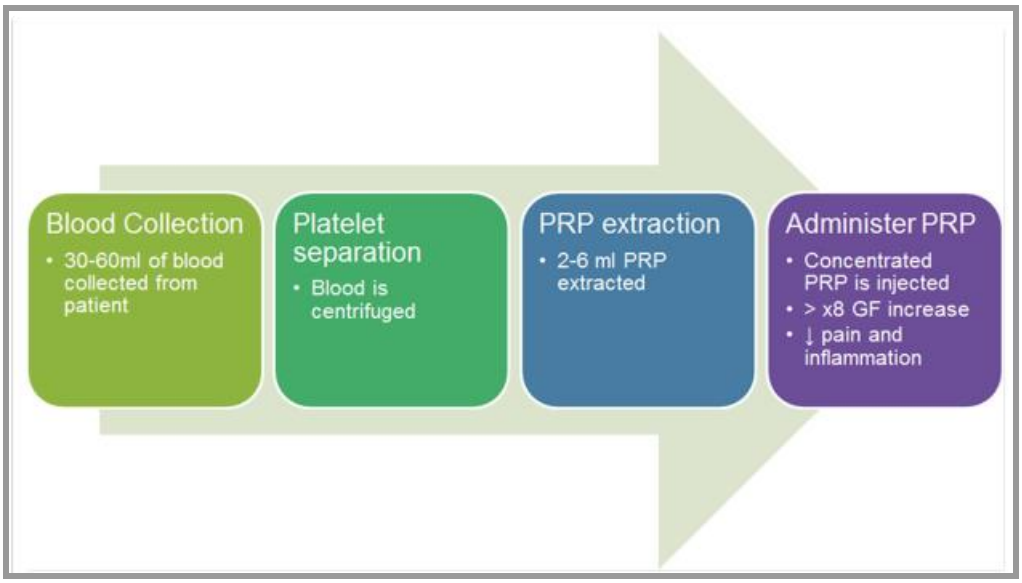


Figure 14: PRP preparation process.[46]

PROCEDURE OF PRP INJECTION

In operation theatre, the patient in supine position, knee was thoroughly scrubbed, & painted after that sterile draping techniques followed. Then the patients knee in slight flexion so that joint is opened for injection using lateral parapatellar approach.

Under sterile aseptic conditions, about 5 mL platelet concentrate was injected into knee joint using 18- gauge needle without using any local anesthetic. Post injection of PRP passive knee movements (flexion and extension) were performed. After the procedure, Jone's compression bandage was applied and the knees were immobilized for ten minutes. Patients were then observed for thirty minutes for possible side effects like sweating, dizziness. During follow-up period, no analgesics were allowed.

Figure 15: Centrifuge for PRP separation with timer on the front side.

Figure 16: Vacutainer inside the centrifuge.

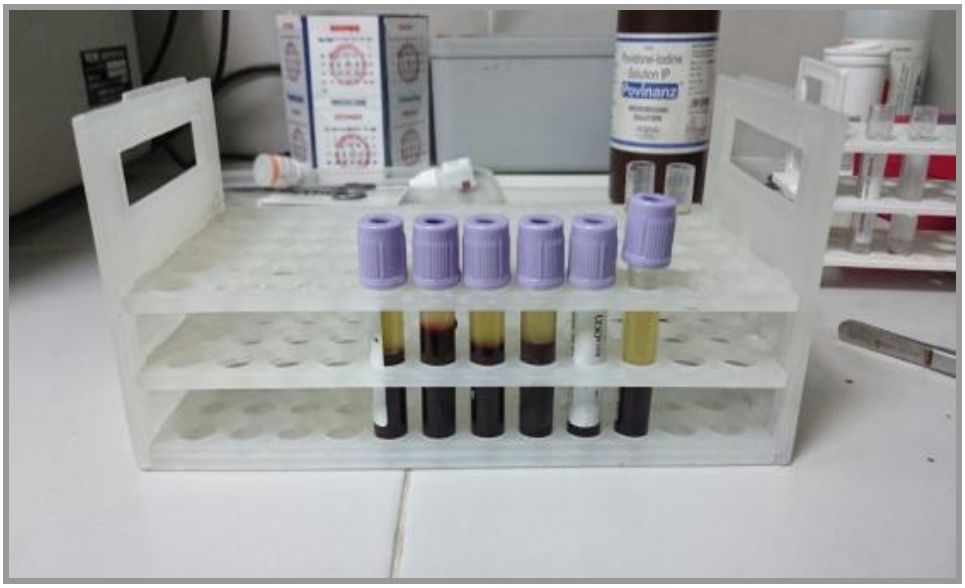


Figure 17: Vacutainers following 15 minutes of centrifuge with 1500 RPM.

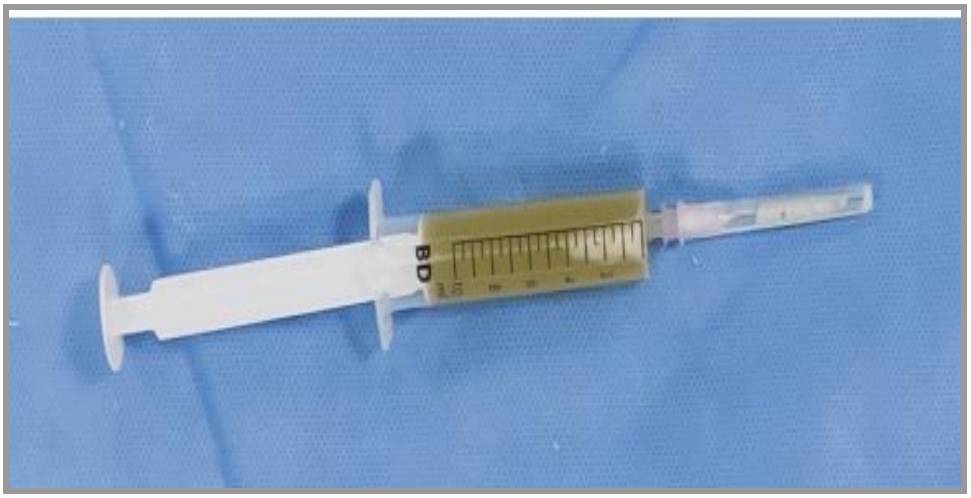


Figure 18: PRP in a 10 ml syringe.

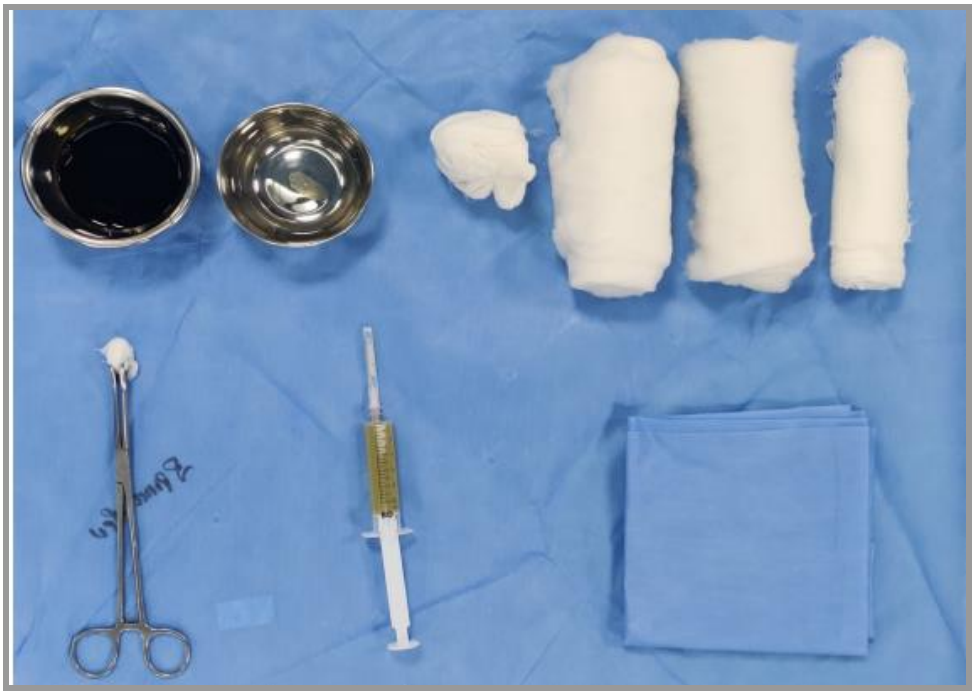


Figure 19: Preparation before injection.

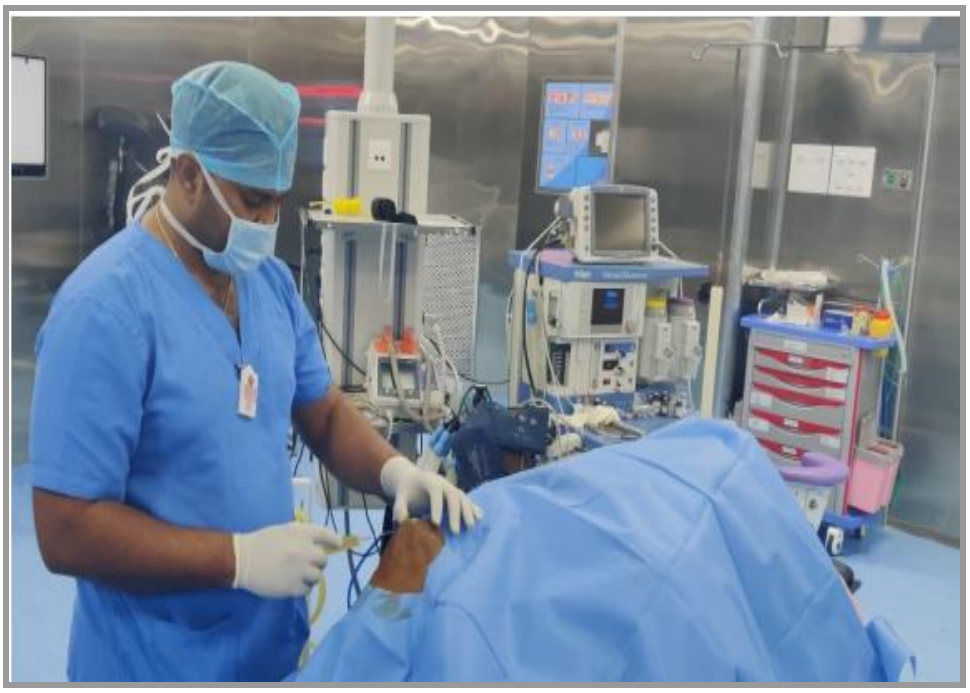


Figure 20: Infiltration of PRP in to knee joint.

Figure 21: Performing flexion & extension of knee after infiltration of PRP.

Figure 22: Application of Jone's compression bandage.

OUTCOME MEASURES

Each patient was allotted a separate WOMAC and VAS chart till complete follow up. Each knee was scored separately, as we were considering each as a separate unit. Initial WOMAC & VAS score were recorded prior to the administration of PRP infiltration i.e. on day '0' and after the infiltration patients were asked to come for review on 1^{st},3^{rd} & 6^{th} months. Decrease in WOMAC & VAS scores was considered as improvement in the patient's condition. WOMAC score was measured in its individual variables and in total.

WOMAC SCORE

In 1982, Nicholas Bellamy had developed a health status questionnaire termed the Western Ontario and McMaster (WOMAC) Osteoarthritis Index. Between 1996 and 1999 the Index underwent significant refinement, a process that has been consolidated between 1999 and the present and has resulted in the 3.1 series of WOMAC questionnaires.[80]

The WOMAC consists of 24 items divided into 3 subscales(components):

- Pain (5 items): during walking, using stairs, in bed, sitting or lying, and standing
- Stiffness (2 items): after first waking and later in the day
- Physical Function (17 items): stair use, rising from sitting, standing, bending, walking, getting in / out of a car, shopping, putting on / taking off socks, rising from bed, lying in bed, getting in / out of bath, sitting, getting on / off toilet, heavy household duties, light household duties.
- in order to suite the WOMAC score with Indian rural population, we had replaced the item getting in/out of a car with getting in/out of auto and putting on/taking off socks with cleaning of ankles.

Each item mentioned in WOMAC scoring system was described in terms of - none, mild moderate, severe, and extreme. These correspond to scale of 0-4. Each component of the WOMAC score ranges between 0-20 for pain, 0-8 for stiffness and 0-68 for functionality. A total WOMAC score was obtained by adding the items for all three subscales, ranges from 0-96.[80]

As we have not found any literature for grading the results of WOMAC score, hence we have graded it to quantify the results. Outcome measured is quantified in percentage of improvement.

85-100% improvement – excellent

70-84% improvement – good

55-69% improvement – fair

< 55% improvement – poor.

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Name:_____ Date:_____

Instructions: Please rate the activities in each category according to the following scale of difficulty: 0 = None, 1 = Slight, 2 = Moderate, 3 = Very, 4 = Extremely

Circle **one number** for each activity

Pain	1. Walking	0	1	2	3	4
	2. Stair Climbing	0	1	2	3	4
	3. Nocturnal	0	1	2	3	4
	4. Rest	0	1	2	3	4
	5. Weight bearing	0	1	2	3	4
Stiffness	1. Morning stiffness	0	1	2	3	4
	2. Stiffness occurring later in the day	0	1	2	3	4
Physical Function	1. Descending stairs	0	1	2	3	4
	2. Ascending stairs	0	1	2	3	4
	3. Rising from sitting	0	1	2	3	4
	4. Standing	0	1	2	3	4
	5. Bending to floor	0	1	2	3	4
	6. Walking on flat surface	0	1	2	3	4
	7. Getting in / out of car/auto	0	1	2	3	4
	8. Going shopping	0	1	2	3	4
	9. Putting on socks/cleaning of ankles	0	1	2	3	4
	10. Lying in bed	0	1	2	3	4
	11. Taking off socks	0	1	2	3	4
	12. Rising from bed	0	1	2	3	4
	13. Getting in/out of bath	0	1	2	3	4
	14. Sitting	0	1	2	3	4
	15. Getting on/off toilet	0	1	2	3	4
	16. Heavy domestic duties	0	1	2	3	4
	17. Light domestic duties	0	1	2	3	4

Total Score: _____ / 96 = _____ %

Comments / Interpretation (to be completed by therapist only):

Figure 23: Chart used to evaluate WOMAC score.[80]

VISUAL ANALOGUE SCALE (VAS)

This tool was first used in psychology by Freyd in 1923. The Visual Analogue Scale (VAS) consists of a straight line with the endpoints defining extreme limits such as ‘no pain at all’ and ‘worst pain’. The patient is asked to mark his pain level on the line between the two endpoints. The distance between ‘no pain at all’ and the mark then defines the subject’s pain.[81]

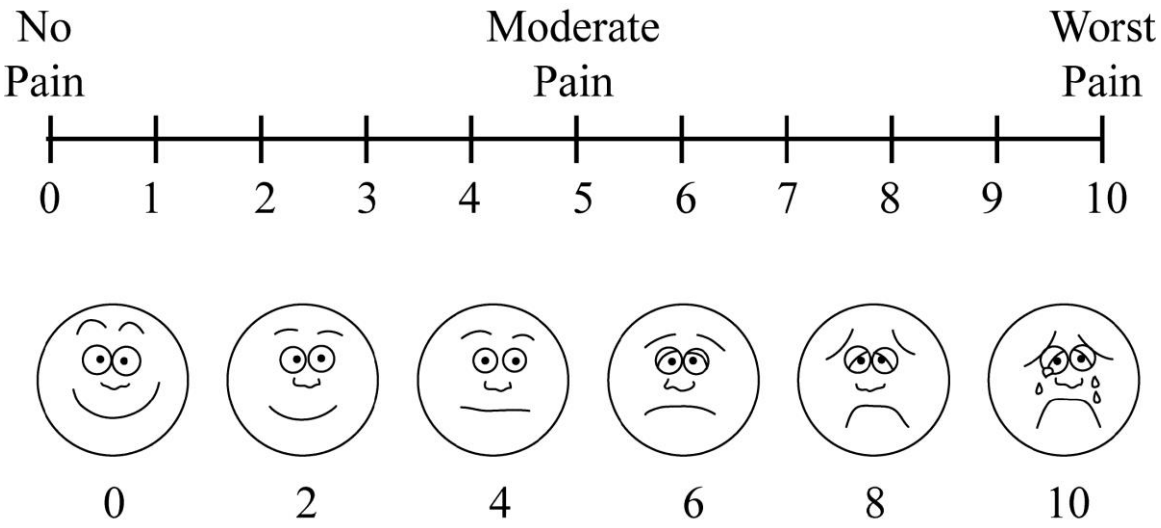


Figure 24: Chart used to evaluate VAS score.[81]

STATISTICAL METHODS

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, **Assumptions: 1.** Dependent variables should be normally distributed, 2. Samples drawn from the population should be random, cases of the samples should be independent

Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, student t test(two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for qualitative data analysis. Fisher Exact test used when cell samples are very small.

Significant figures .

+ Suggestive significance (P value: $0.05<P<0.10$)

* Moderately significant (P value:$0.01<P \leq 0.05$)

** Strongly significant (P value: $P \leq 0.01$)

Statistical software:

The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and microsoft word and excel have been used to generate graphs, tables etc**.**

RESULTS AND OBSERVATIONS

Table 7: Age distribution.

Age in years	No. of patients	Percentage (%)
40-50	21	35.0
51-60	16	26.7
61-70	15	25.0
>70	8	13.3
Total	60	100.0

The mean age of subjects in the study was 57.87±11.15 years.

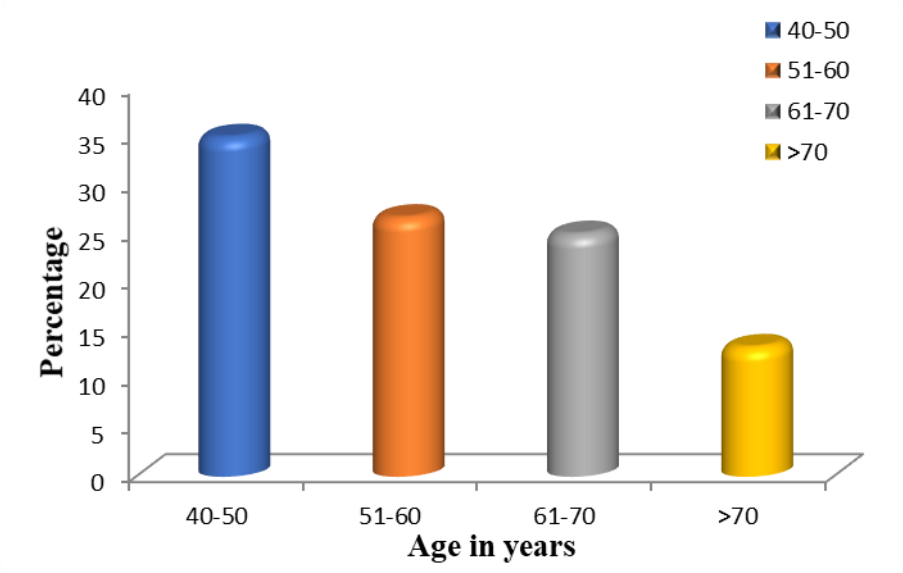


Chart 1: Bar diagram showing Age.

Table 8: Gender distribution.

Gender	No. of patients	Percentage (%)
Female	36	60.0
Male	24	40.0
Total	60	100.0

Majority of the patients were females (60%)

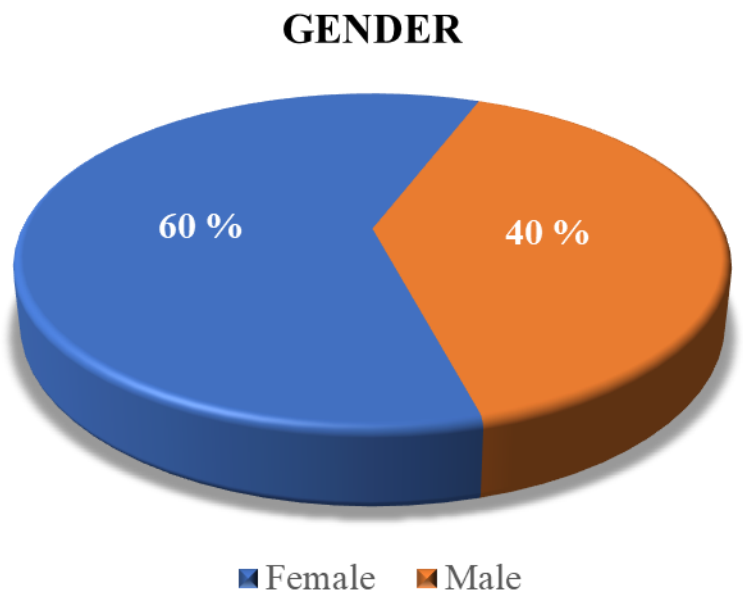


Chart 2: Gender distribution.

Table 9: Knee Joint involved.

Knee Joint Side	No. of patients	Percentage (%)
Left	22	36.7
Right	38	63.3
Total	60	100.0

Right side (63.3 %) was more commonly involved than left (36.7).

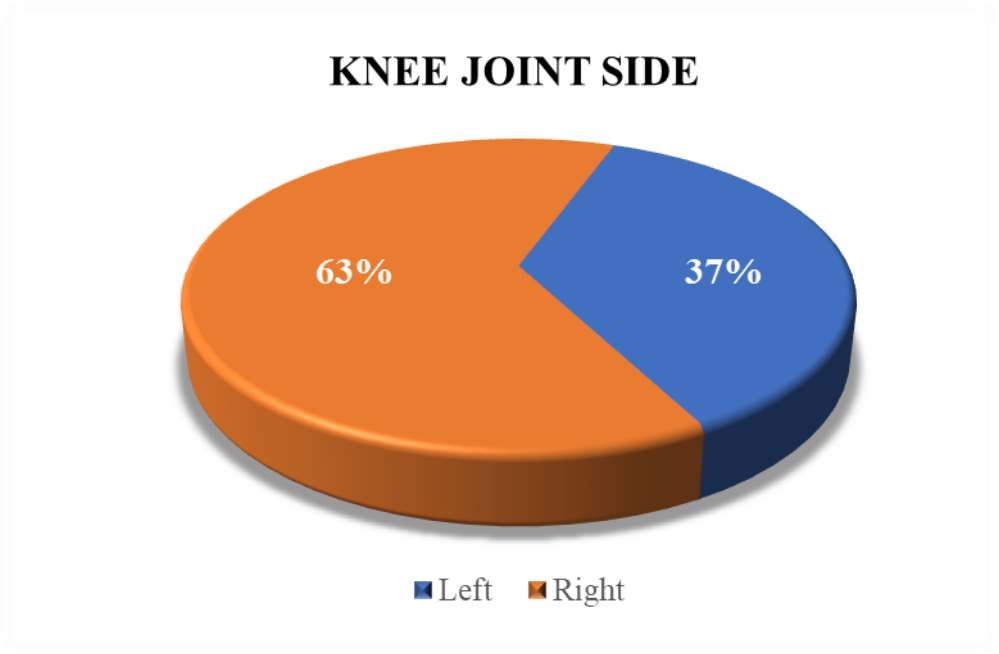


Chart 3: Knee Joint involved.

Table 10: Grade of Osteoarthritis.

Grade OA	No. of patients	Percentage (%)
I	23	38.3
II	37	61.7
Total	60	100.0

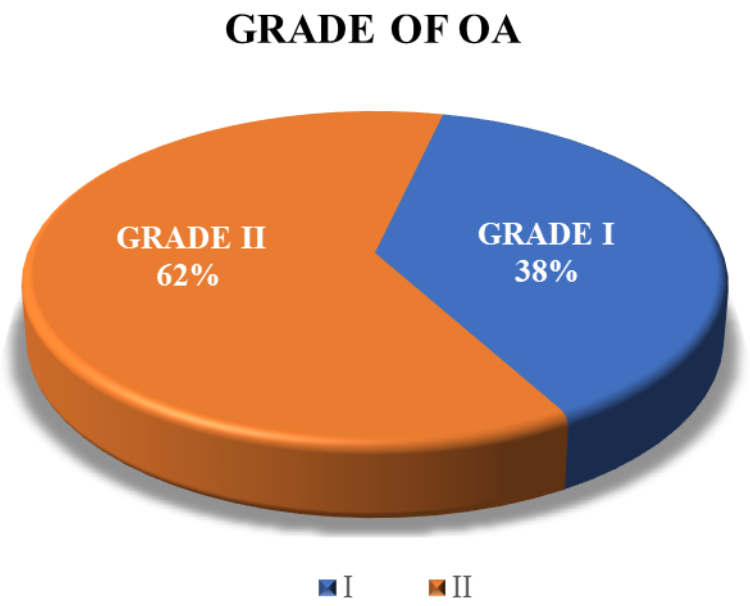


Chart 4: Grade of Osteoarthritis.

Table 11: VAS Score.

VAS Score	0 day	1 month	3 months	6 months	Percentage (%) difference
0	0(0%)	0(0%)	0(0%)	0(0%)	0.0%
1-3	0(0%)	0(0%)	16(26.7%)	48(80%)	80.0%
4-6	16(26.7%)	56(93.3%)	43(71.7%)	12(20%)	-6.7%
7-10	44(73.3%)	4(6.7%)	1(1.7%)	0(0%)	-73.3%
Total	60(100%)	60(100%)	60(100%)	60(100%)	-

P<0.001**, Significant, paired Proportion test, 80% improvement in lowest VAS score.

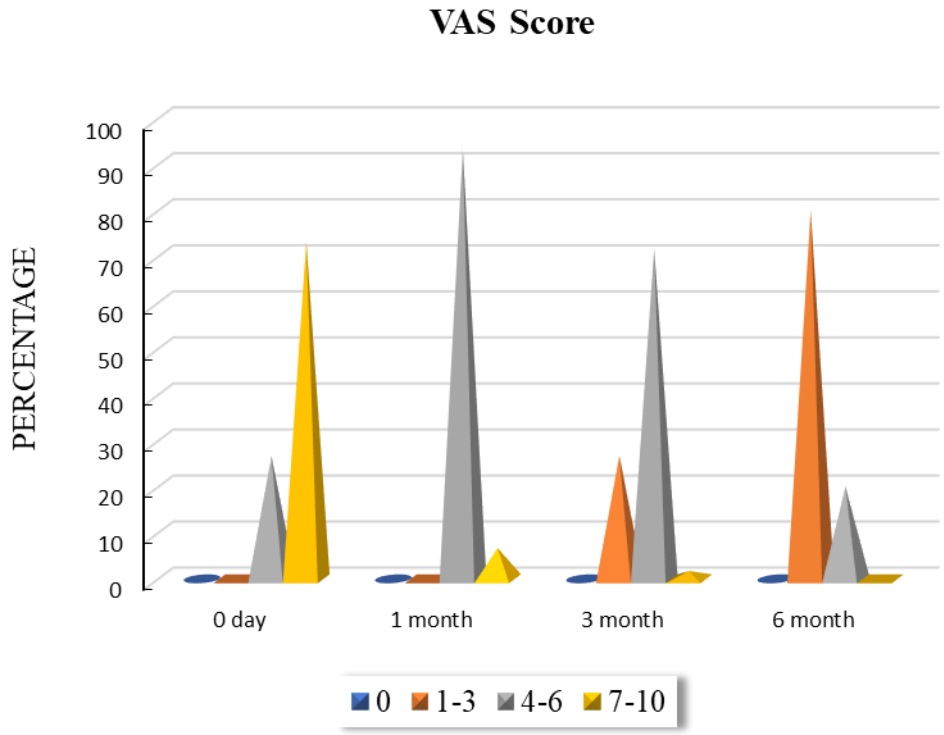


Chart 5: Bar diagram showing VAS Score.

Table 12: Mean VAS Score.

VAS Score	Min-Max	Mean ± SD	difference	t value	P value
0 day	6.00-8.00	7.08±0.79	-	-	-
1 month	4.00-7.00	5.37±0.76	1.717	27.121	<0.001**
3 months	2.00-7.00	4.07±0.97	3.017	27.377	<0.001**
6 months	1.00-6.00	2.78±1.22	4.300	27.492	<0.001**

Student t test (paired)

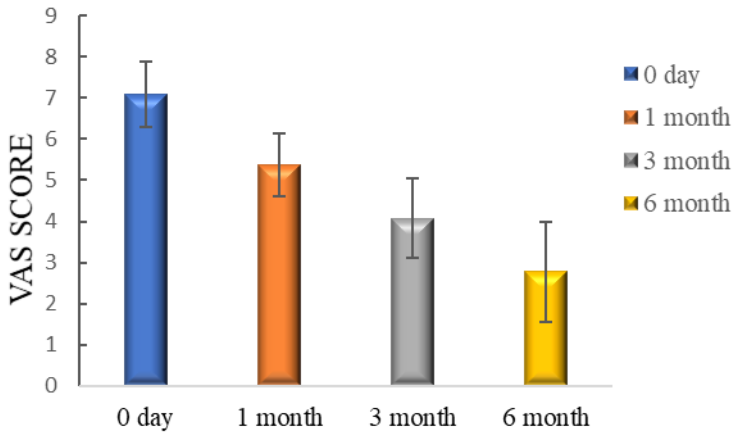


Chart 6A: Bar diagram showing Mean VAS Score.

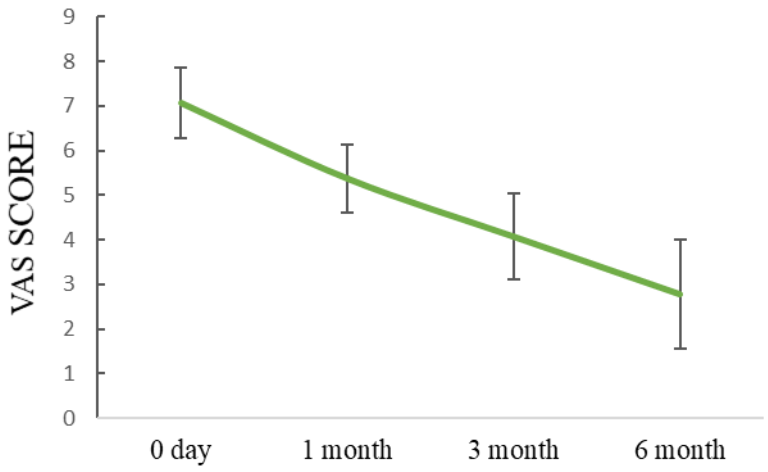


Chart 6B: Graph showing Mean VAS Score.

Table 13: Mean WOMAC Pain.

WOMAC Pain	Min-Max	Mean ± SD	difference	t value	P value
0 day	7.00-19.00	14.53±2.36	-	-	-
1 month	5.00-17.00	10.82±2.25	3.717	22.317	<0.001**
3 months	3.00-14.00	7.58±2.32	6.950	29.473	<0.001**
6 months	1.00-12.00	4.68±2.67	9.850	31.800	<0.001**

Student t test (paired)

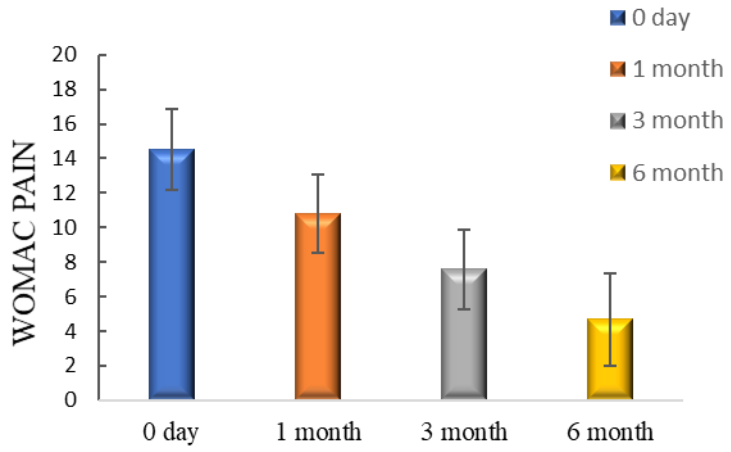


Chart 7A: Bar diagram showing Mean WOMAC Pain.

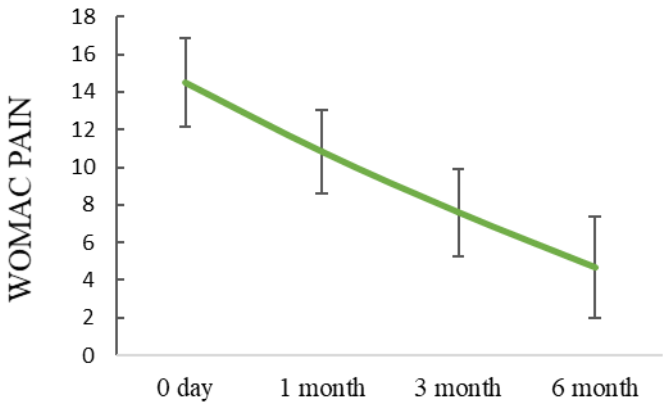


Chart 7B: Graph showing Mean WOMAC Pain.

Table 14: Mean WOMAC Stiffness.

W0MAC Stiffness	Min-Max	Mean ± SD	difference	t value	P value
0 day	1.00-8.00	4.70±1.15	-	-	-
1 month	1.00-5.00	3.43±0.87	1.267	12.976	<0.001**
3 months	0.00-5.00	2.38±0.90	2.317	19.694	<0.001**
6 months	0.00-4.00	1.37±0.94	3.333	24.537	<0.001**

Student t test (paired)

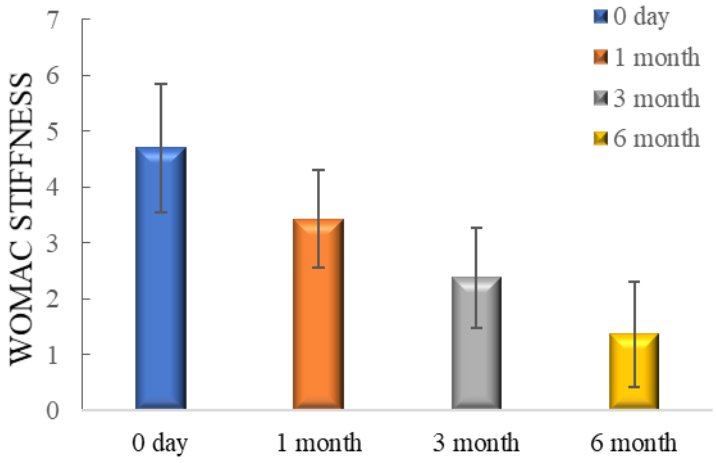


Chart 8A: Bar diagram showing Mean WOMAC Stiffness.

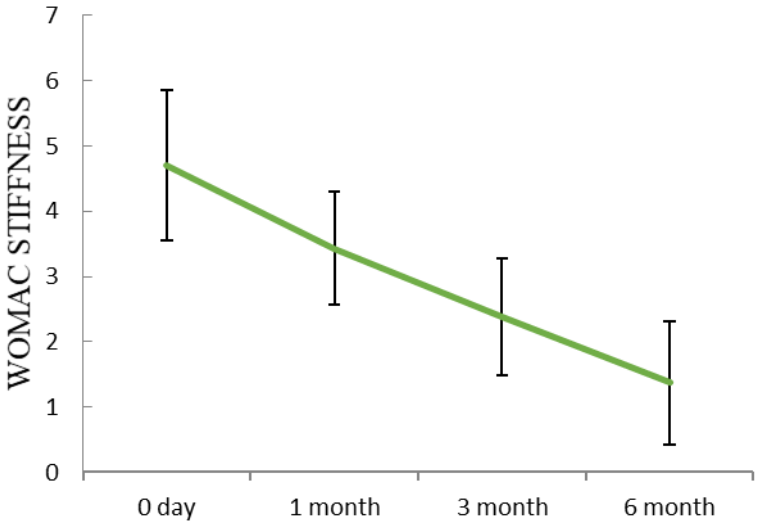


Chart 8B: Graph showing Mean WOMAC Stiffness.

Table 15: Mean WOMAC Functionality.

WOMAC Functionality	Min-Max	Mean ± SD	difference	t value	P value
0 day	36.00-62.00	46.98±5.57	-	-	-
1 month	26.00-51.00	34.72±5.58	12.267	21.524	<0.001**
3 months	11.00-46.00	23.82±6.97	23.167	26.654	<0.001**
6 months	4.00-40.00	13.90±8.70	33.083	28.427	<0.001**

Student t test (paired)

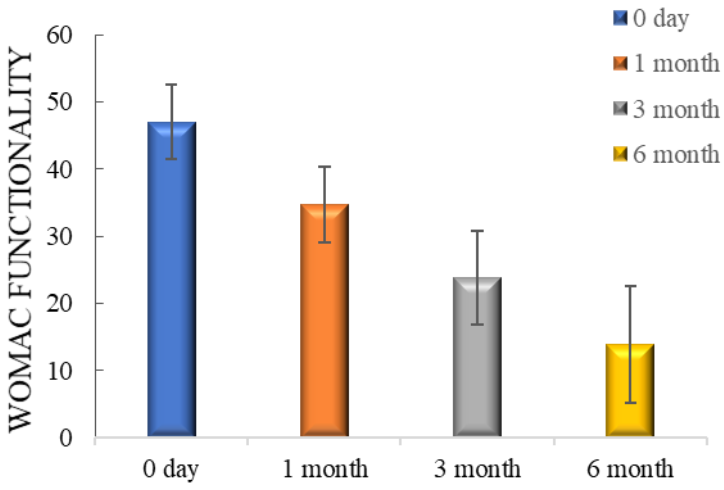


Chart 9A: Bar diagram showing Mean WOMAC Functionality.

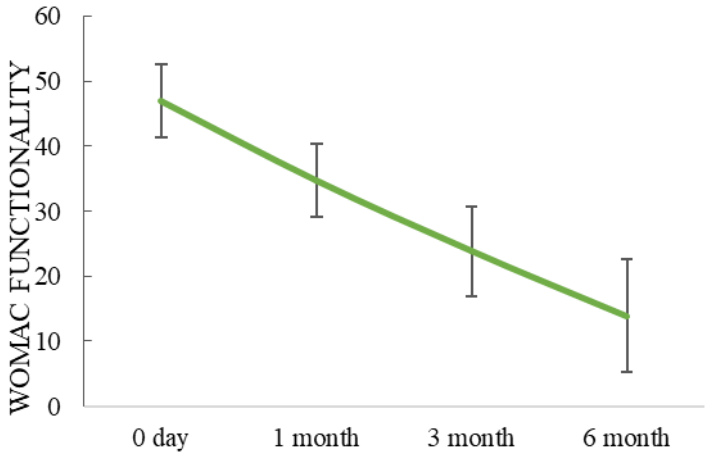


Chart 9B: Graph showing Mean WOMAC Functionality.

Table 16: Mean WOMAC Total.

WOMAC Total	Min-Max	Mean ± SD	difference	t value	P value
0 day	44.00-83.00	66.20±7.63	-	-	-
1 month	32.00-73.00	48.97±7.82	17.233	23.643	<0.001**
3 months	18.00-63.00	33.78±9.55	32.427	30.350	<0.001**
6 months	7.00-54.00	19.95±11.69	46.250	31.700	<0.001**

Student t test (paired)

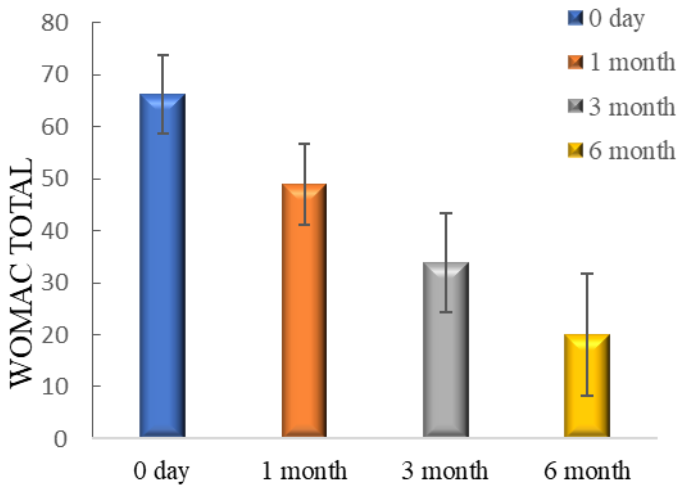


Chart 10A: Bar diagram showing Mean WOMAC Total.

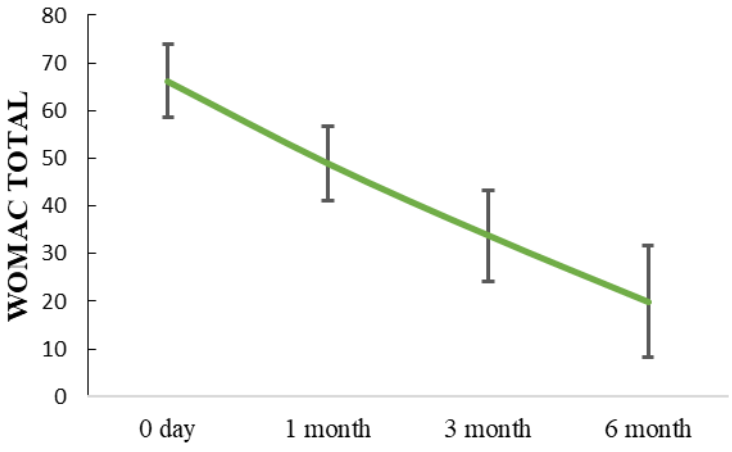


Chart 10B: Graph showing Mean WOMAC Total.

Table 17: Comparison of VAS score, in relation to Grade of OA.

VAS SCORE	Grade of OA		Total	P value
	Grade I	Grade II		
0 day	6.78±0.67	7.27±0.80	7.08±0.79	0.018*
1 month	5.09±0.51	5.54±0.84	5.37±0.76	0.023*
3 months	3.70±0.88	4.30±0.97	4.07±0.97	0.018*
6 months	2.17±0.89	3.16±1.26	2.78±1.22	0.002**

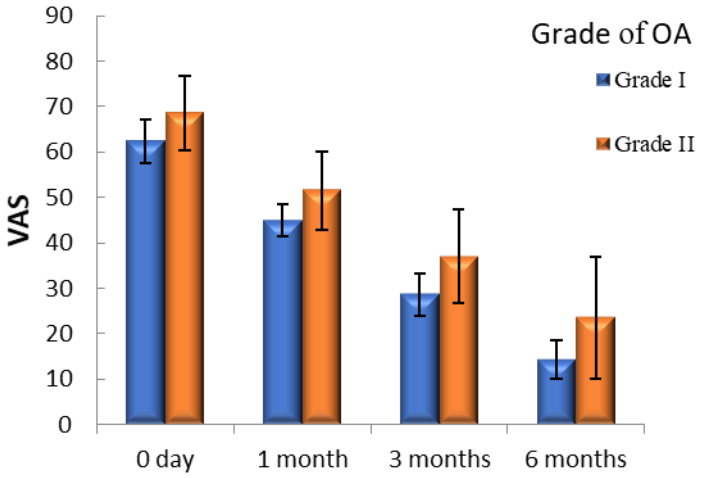


Chart 11A: Bar diagram showing Comparison of VAS score, in relation to Grade.

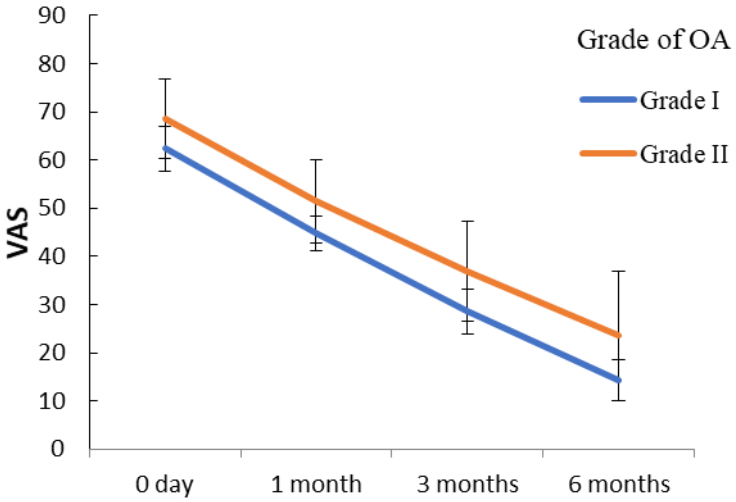


Chart 11B: Graph showing Comparison of VAS score, in relation to Grade of OA.

Table 18: Comparison of WOMAC PAIN score, in relation to Grade of OA.

WOMAC pain	Grade of OA		Total	P value
	Grade I	Grade II		
0 day	13.74±1.74	15.03±2.58	14.53±2.36	0.039*
1 month	9.87±1.49	11.41±2.45	10.82±2.25	0.009**
3 months	6.61±1.20	8.19±2.64	7.58±2.32	0.009**
6 months	3.35±1.15	5.51±3.01	4.68±2.67	0.002**

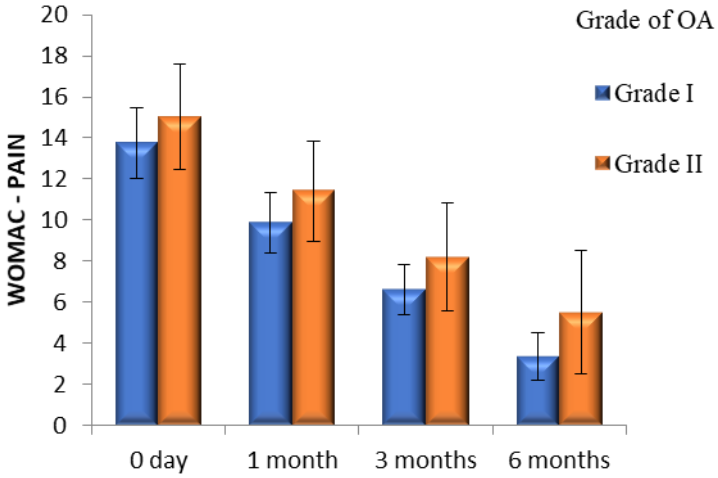


Chart 12A: Bar diagram showing Comparison of WOMAC PAIN score, in relation to Grade of OA.

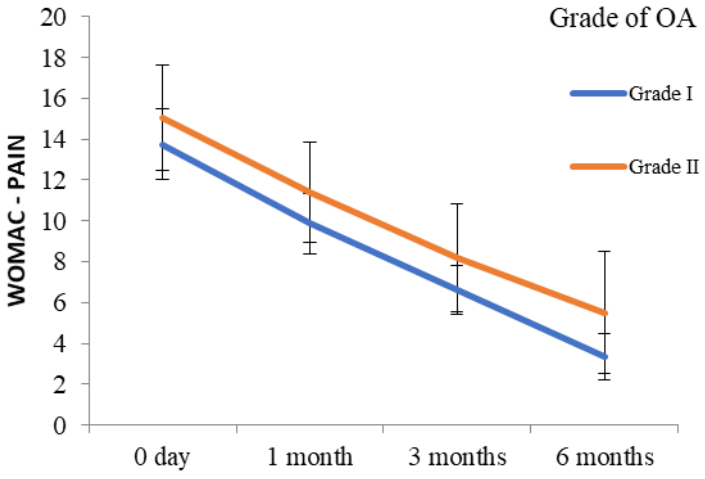


Chart 12B: Graph showing Comparison of WOMAC PAIN score, in relation to Grade of OA.

Table 19: Comparison of WOMAC STIFFNESS score, in relation to Grade of OA.

WOMAC Stiffness	Grade of OA		Total	P value
	Grade I	Grade II		
0 day	4.39±0.99	4.89±1.22	4.70±1.15	0.103
1 month	3.17±0.72	3.59±0.93	3.43±0.87	0.068+
3 months	2.04±0.56	2.59±1.01	2.38±0.90	0.020*
6 months	0.96±0.64	1.62±1.01	1.37±0.94	0.007**

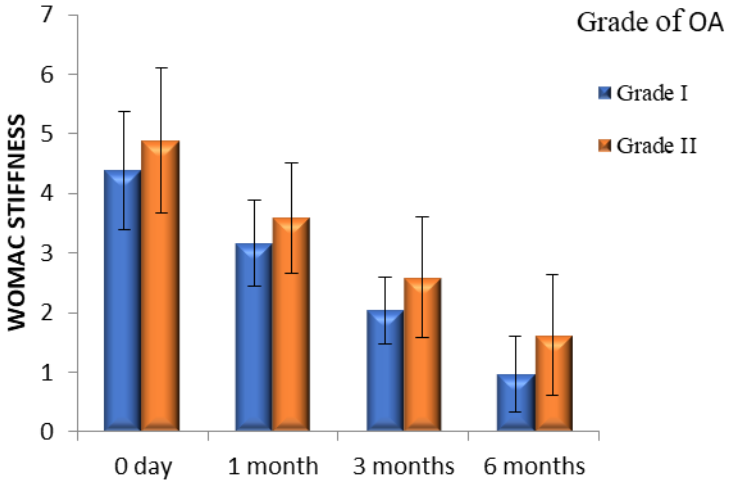


Chart 13A: Bar diagram showing Comparison of WOMAC STIFFNESS score, in relation to Grade of OA.

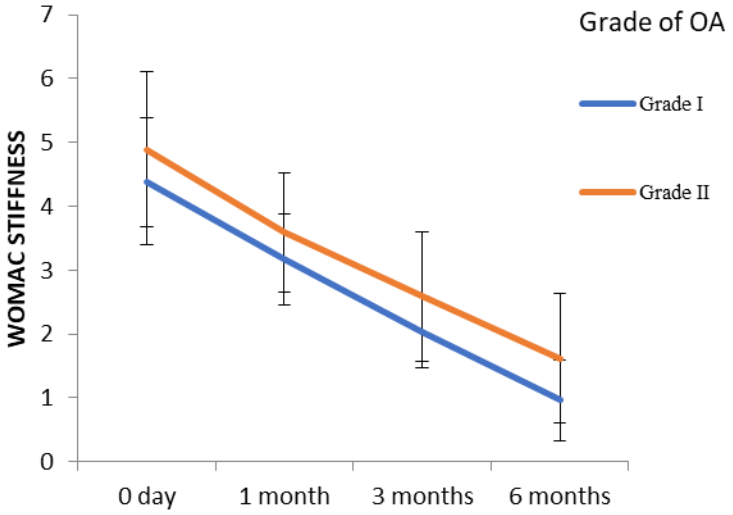


Chart 13B: Graph showing Comparison of WOMAC STIFFNESS score, in relation to Grade of OA.

Table 20: Comparison of WOMAC FUNCTIONALITY score, in relation to Grade of OA.

WOMAC FUNCTIONALITY	Grade of OA		Total	P value
	Grade I	Grade II		
• 0 day	44.22±3.66	48.70±5.90	46.98±5.57	0.002**
• 1 month	31.78±2.61	36.54±6.15	34.72±5.58	0.001**
• 3 months	19.91±3.72	26.24±7.44	23.82±6.97	<0.001**
• 6 months	9.91±3.15	16.38±10.08	13.90±8.70	0.004**

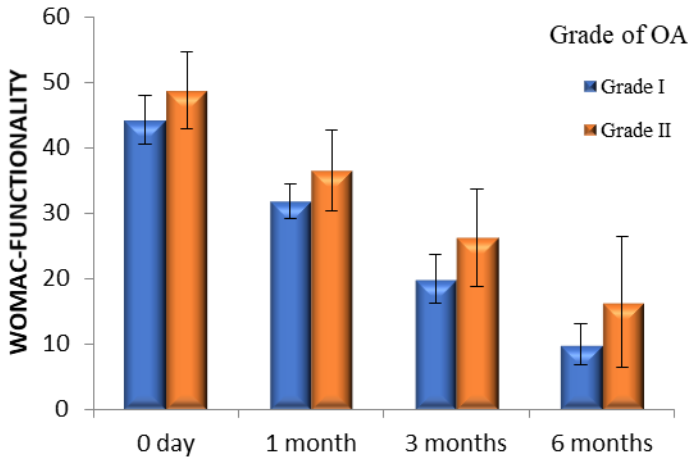


Chart 14A: Bar diagram showing Comparison of WOMAC FUNCTIONALITY score, in relation to Grade of OA.

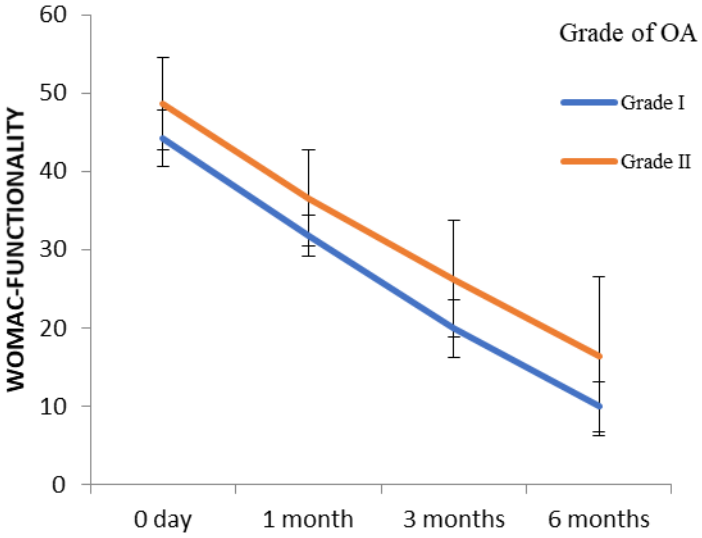


Chart 14B: Graph showing Comparison of WOMAC FUNCTIONALITY score, in relation to Grade of OA.

Table 21: Comparison of WOMAC TOTAL score, in relation to Grade of OA in patients.

WOMAC TOTAL	Grade of OA		Total	P value
	Grade I	Grade II		
• 0 day	62.35±4.68	68.59±8.16	66.20±7.63	0.001**
• 1 month	44.83±3.54	51.54±8.65	48.97±7.82	0.001**
• 3 months	28.57±4.68	37.03±10.39	33.78±9.55	0.001**
• 6 months	14.22±4.26	23.51±13.38	19.95±11.69	0.002**

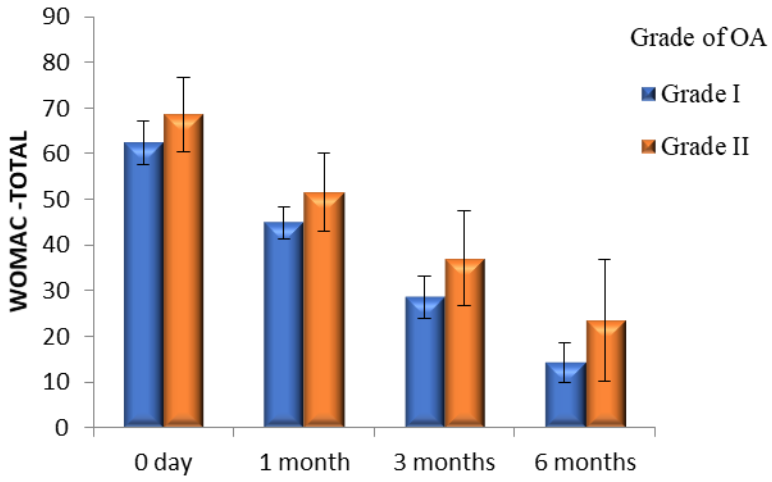


Chart 15A: Bar diagram showing Comparison of WOMAC TOTAL score, in relation to Grade of OA in patients.

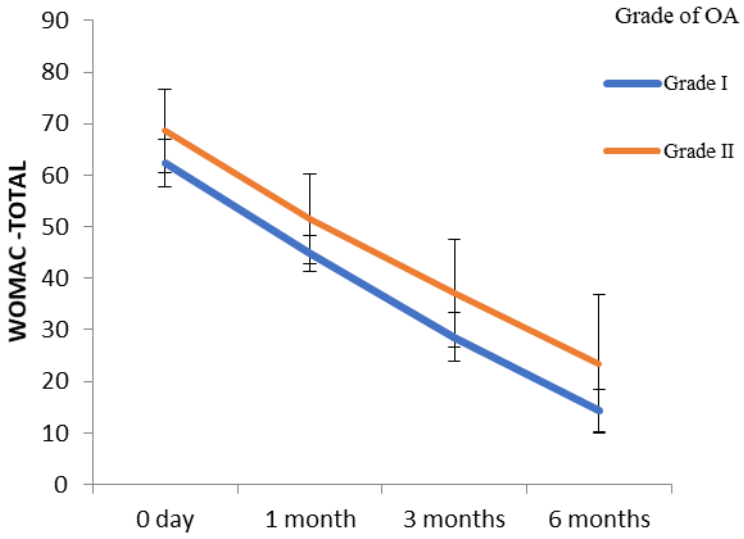


Chart 15B: Bar diagram showing Comparison of WOMAC TOTAL score, in relation to Grade of OA in patients.

Table 22: Comparison of WOMAC PAIN score, in relation to Grade of results.

WOMAC PAIN	Grade Result				P value
	Excellent	Good	Fair	Poor	
0 day	13.33±1.97	14.14±2.45	14.78±2.18	16.57±1.72	0.046*
1 month	9.33±1.75	10.07±1.75	11.00±1.53	14.71±1.89	<0.001**
3 months	5.67±1.75	6.69±1.39	7.83±1.47	12.29±1.38	<0.001**
6 months	2.33±0.82	3.34±1.26	5.44±1.54	10.29±1.70	<0.001**

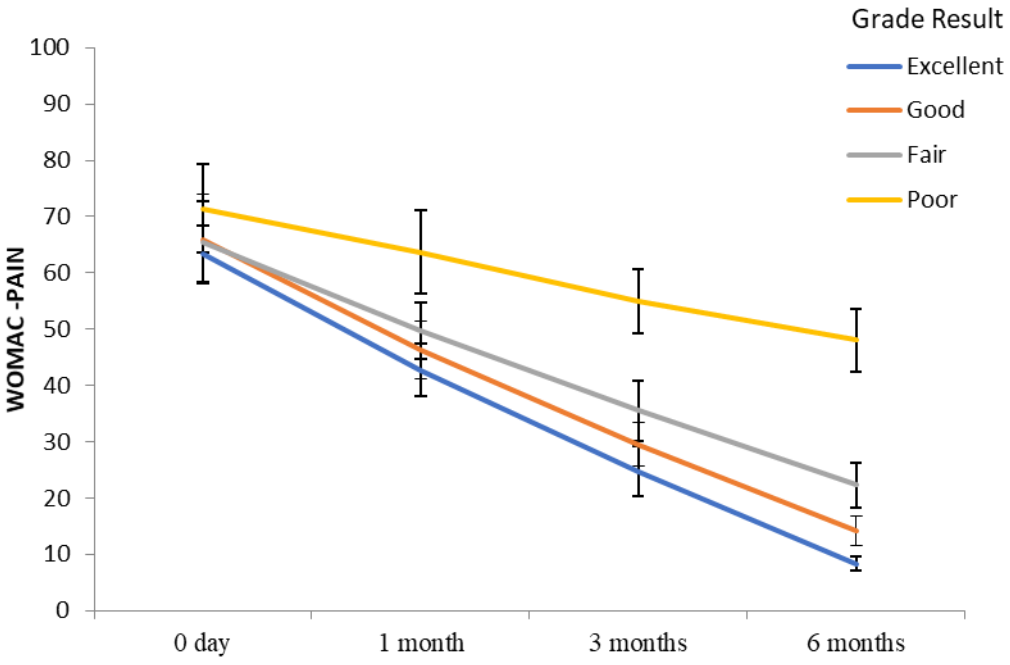


Chart16: Graph diagram showing Comparison of WOMAC PAIN score, in relation to Grade of results.

Table 23: Comparison of WOMAC STIFFNESS score, in relation to Grade of results.

WOMAC STIFFNESS	Grade Result				P value
	Excellent	Good	Fair	Poor	
0 day	4.67±0.52	4.55±1.18	4.72±1.07	5.29±1.60	0.524
1 month	3.00±0.00	3.21±0.86	3.67±0.69	4.14±1.21	0.020*
3 months	1.67±0.52	2.14±0.69	2.67±0.77	3.29±1.38	0.001**
6 months	0.50±0.55	1.07±0.59	1.67±0.59	2.57±1.62	<0.001**

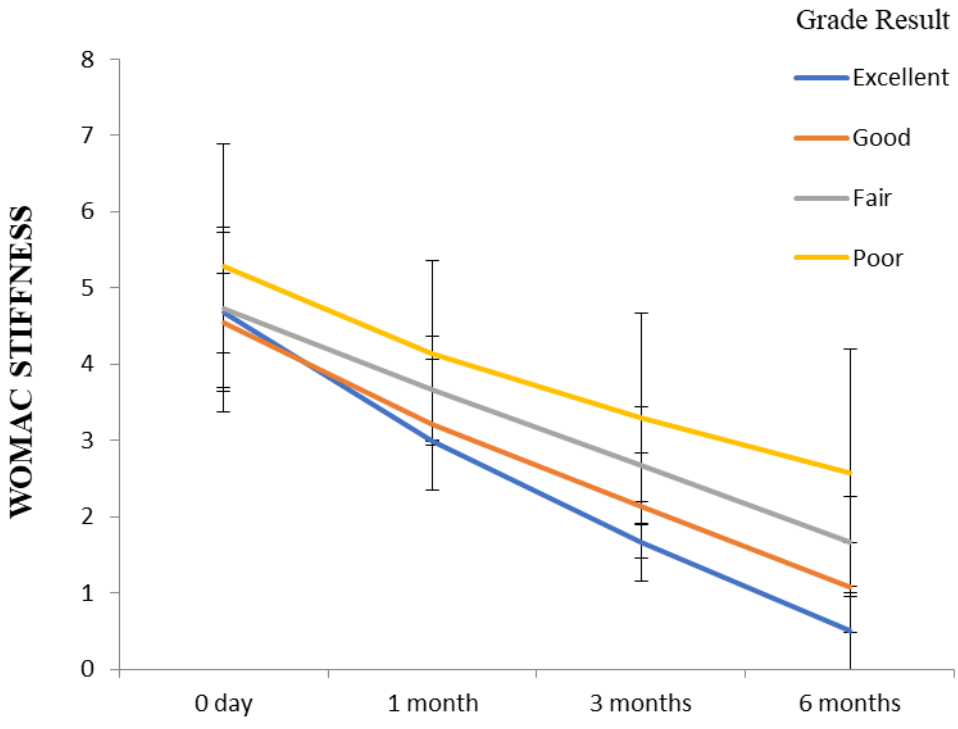


Chart 17: Graph diagram Comparison of WOMAC STIFFNESS score, in relation to Grade of results.

Table 24: Comparison of WOMAC FUNCTIONALITY score, in relation to Grade of results

WOMAC FUNTIONALITY	Grade Result				P value
	Excellent	Good	Fair	Poor	
0 day	45.33±3.44	47.28±5.74	46.06±5.25	49.57±7.04	0.464
1 month	30.33±3.27	33.00±3.77	35.00±3.87	44.86±5.87	<0.001**
3 months	17.33±3.61	20.69±2.98	25.00±3.56	39.29±4.07	<0.001**
6 months	5.50±1.22	9.72±1.91	15.17±2.62	35.14±4.53	<0.001**

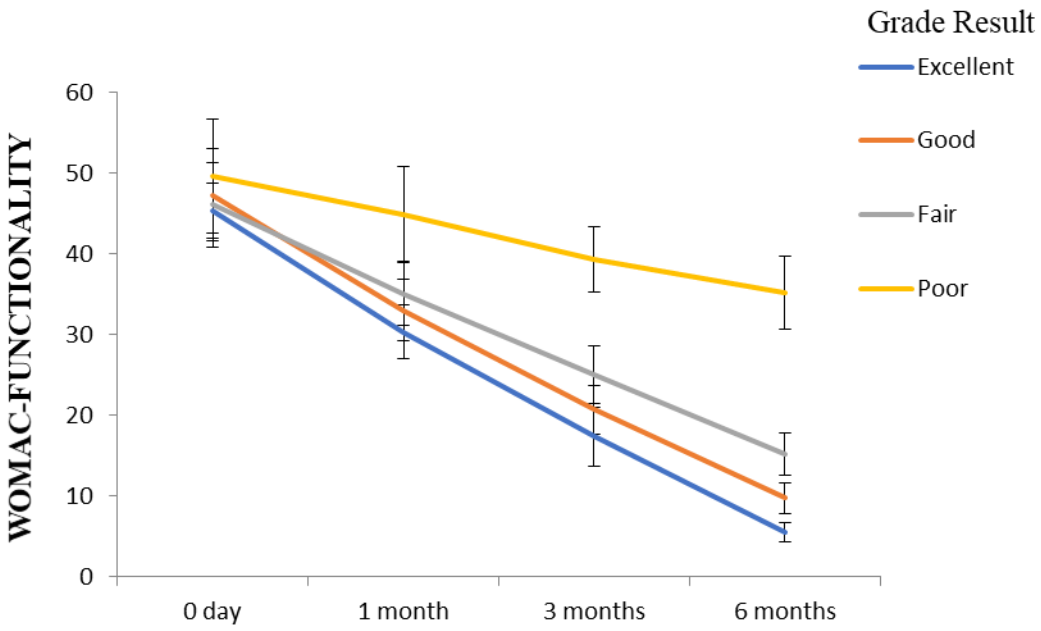


Chart 18: Comparison of WOMAC FUNCTIONALITY score, in relation to Grade of results.

Table 25: Comparison of WOMAC TOTAL score, in relation to Grade of results.

WOMAC TOTAL	Grade Result				P value
	Excellent	Good	Fair	Poor	
0 day	63.33±5.16	65.97±8.04	65.5±7.13	71.43±7.89	0.232
1 month	42.67±4.68	46.28±5.21	49.67±5.03	63.71±7.39	<0.001**
3 months	24.67±4.46	29.52±3.84	35.50±5.34	54.86±5.70	<0.001**
6 months	8.33±1.21	14.14±2.71	22.28±4.03	48.00±5.57	<0.001**

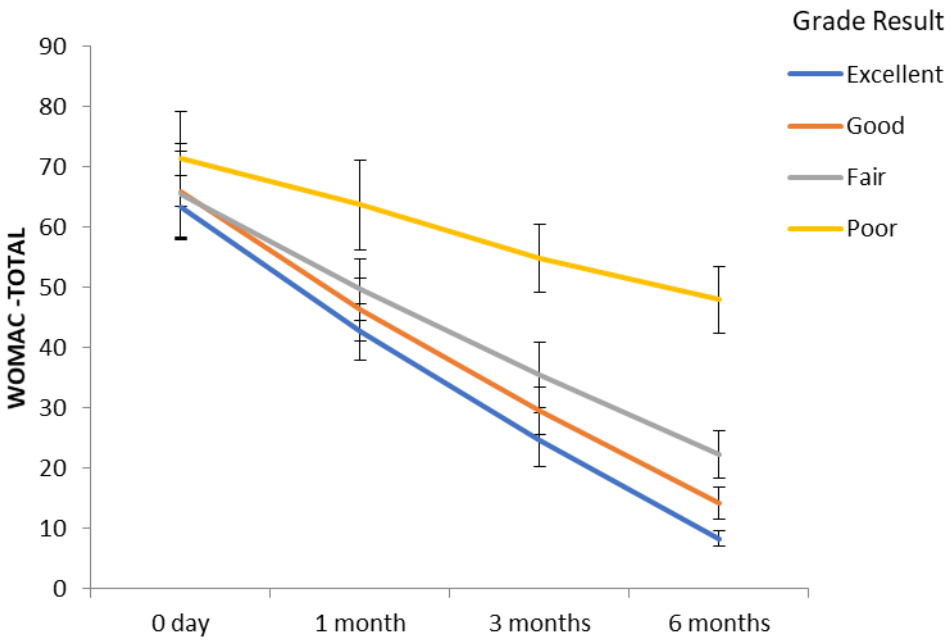


Chart 19: Comparison of WOMAC TOTAL score, in relation to Grade of results.

Table 26: Percentage of Improvement in relation to Grade of OA.

Percentage (%) of Improvement	Grade of OA		Total
	Grade I	Grade II	
1-25	0(0%)	0(0%)	0(0%)
25-50	0(0%)	7(18.9%)	7(11.7%)
51-75	9(39.1%)	16(43.2%)	25(41.7%)
75-100	14(60.9%)	14(37.8%)	28(46.7%)
Total	23(100%)	37(100%)	60(100%)
Mean ± SD	76.89±7.74	66.03±18.03	70.19±15.78

P=0.008**, Significant, Student t test

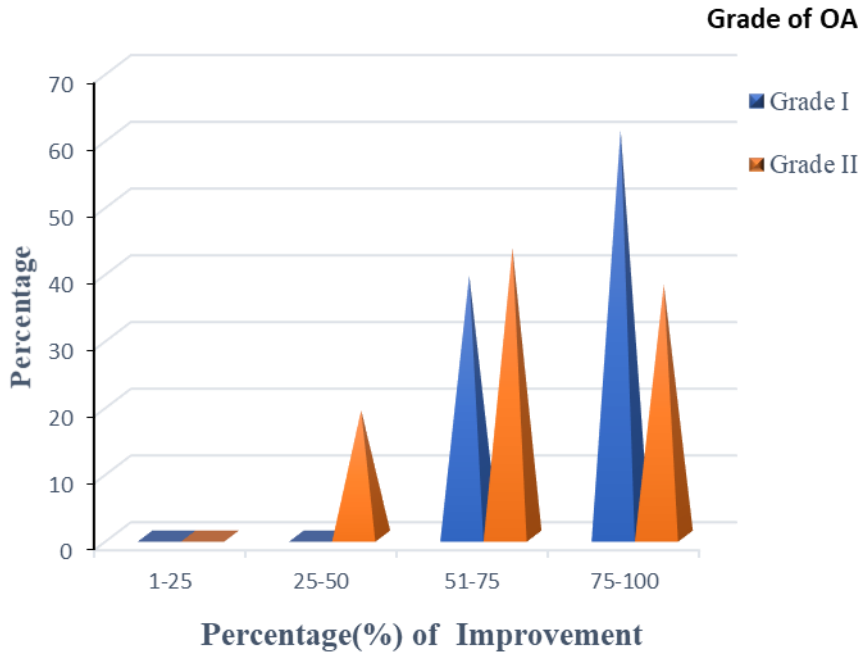


Chart 20: Bar diagram showing Percentage of Improvement in relation to Grade of OA.

Table 27: Grade of Results in relation to Grade of OA.

Grade of Result	Grade of OA		Total
	Grade I	Grade II	
Excellent	5(21.7%)	1(2.7%)	6(10%)
Good	13(56.5%)	16(43.2%)	29(48.3%)
Fair	5(21.7%)	13(35.1%)	18(30%)
Poor	0(0%)	7(18.9%)	7(11.7%)
Total	23(100%)	37(100%)	60(100%)

P=0.010**, Significant, Fisher Exact Test

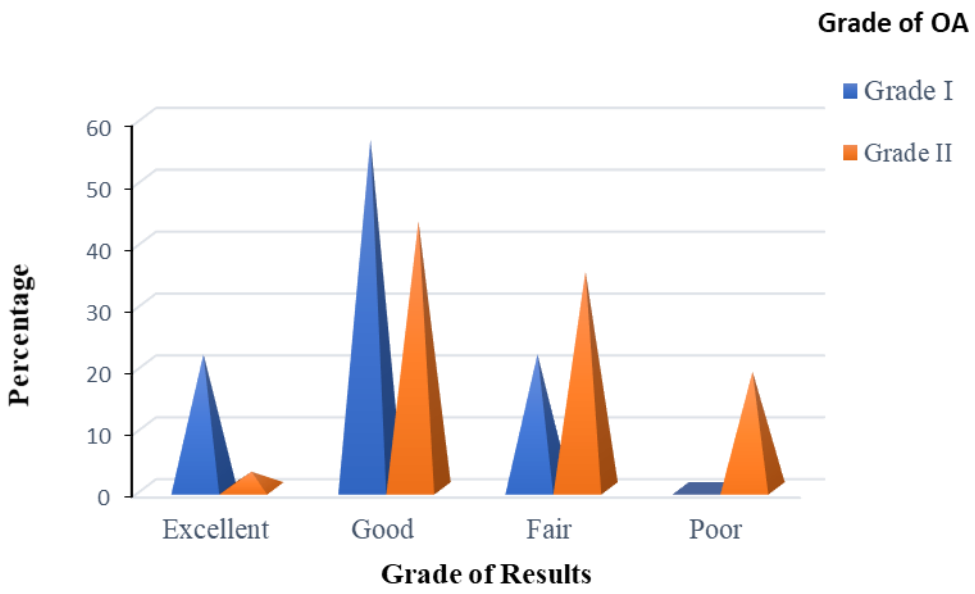


Chart 21: Bar diagram showing Grade of Results in relation to Grade of OA.

Table 28: Percentage of Improvement in TOTAL subjects.

Percentage of Improvement	No. of patients	Percentage (%)
1-25	0	0.0
25-50	7	11.7
51-75	25	41.7
75-100	28	46.7
Total	60	100.0

Mean ± SD: 70.19±15.78

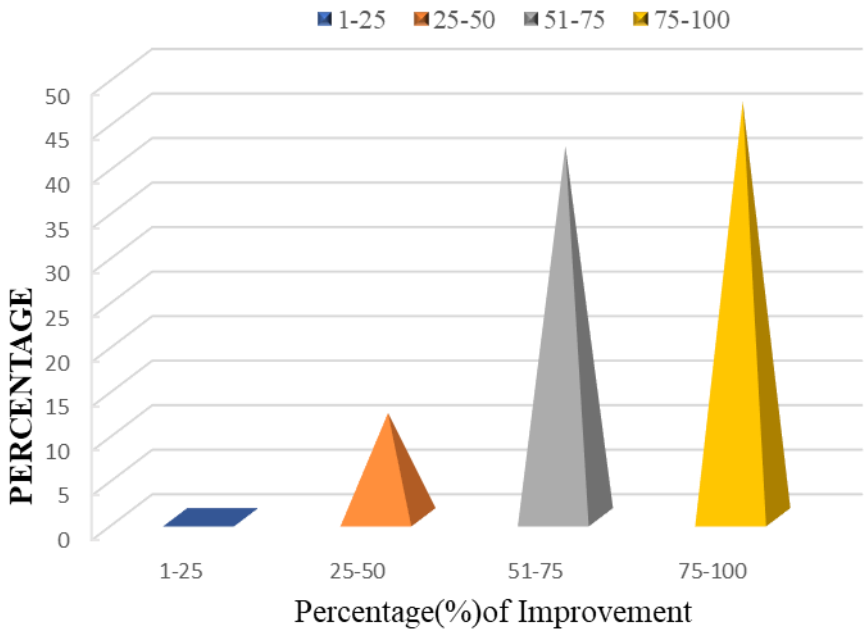


Chart 22: Bar diagram showing Percentage of Improvement in TOTAL subjects.

Table 29: Grade of Result in total subjects.

Grade Result	No. of patients	%
Excellent	6	10.0
Good	29	48.3
Fair	18	30.0
Poor	7	11.7
Total	60	100.0

Chart 23: Bar diagram showing Grade of Result in total subjects.

CASES

CASE NO - 40

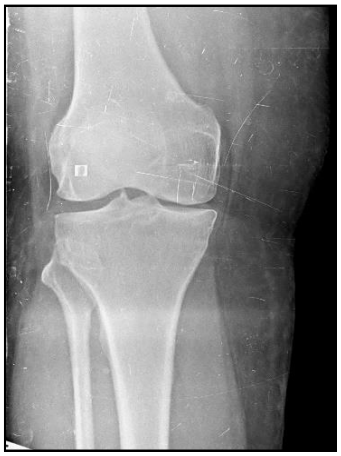
Age: 46 years

Sex: Female

UHID No.: 660403

Diagnosis: Osteoarthritis of Right Knee Grade-II

Date of Inflitraion: 11-12-2018



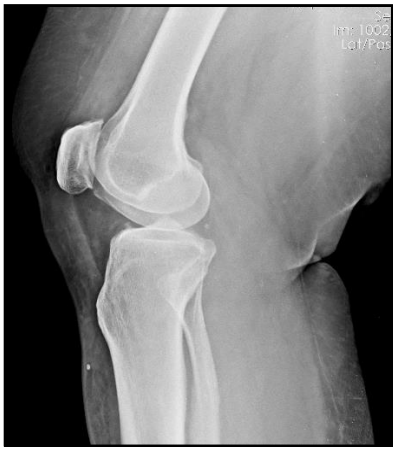


Table 30: VAS and WOMAC TOTAL SCORE of case I

	VAS SCORE	WOMAC PAIN SCORE	WOMAC STIFFNESS SCORE	WOMAC FUNTIONALITY SCORE	WOMAC TOTAL SCORE
'0' day	6	10	5	42	57
1st month	5	7	3	30	40
3rd month	4	3	2	19	24
6th month	2	1	1	5	7

PERCENTAGE (%) OF IMPROVEMENT: **87.71%**

GRADE OF RESULT**: EXCELLENT.**

CASE NO - 4

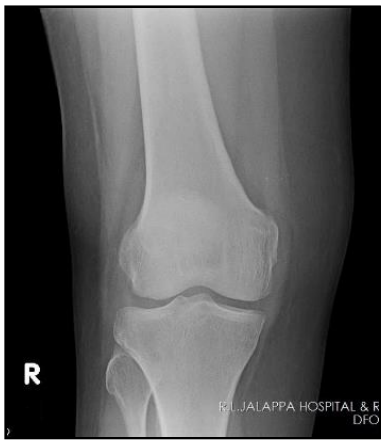
Age: 45 years

Sex: Female

UHID No.: 420791

Diagnosis: Osteoarthritis of Right. Knee Grade-I

Date of Inflitraion: 30-01-2018



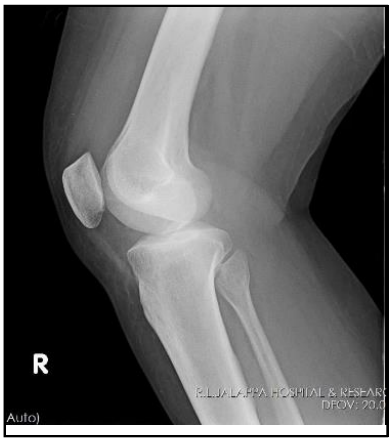


Table 31: VAS and WOMAC TOTAL SCORE of case II

	VAS SCORE	**WOMAC PAIN SCORE**	**WOMAC STIFFNESS SCORE**	**WOMAC FUNTIONALITY SCORE**	**WOMAC TOTAL SCORE**
'0' day	7	13	5	44	62
1st month	6	11	4	36	51
3rd month	5	6	3	25	34
6th month	3	4	1	10	15

PERCENTAGE (%) OF IMPROVEMENT: **75.81%**

GRADE OF RESULT: **GOOD**

CASE NO - 20

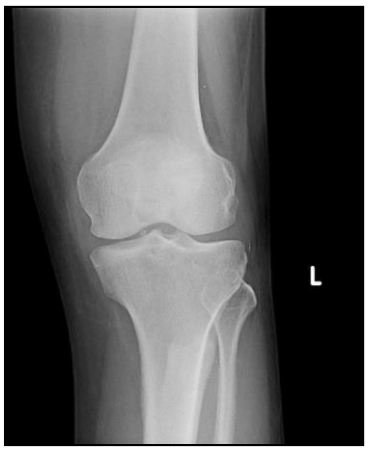
Age: 56 years

Sex: Male

UHID : 319767

Diagnosis: Osteoarthritis of Left Knee Grade-I

Date of Inflitraion: 23-07-2018



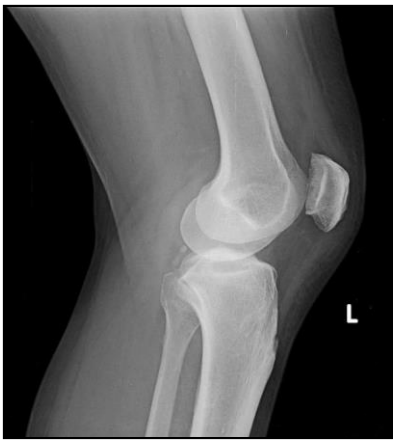


Table 32: VAS and WOMAC TOTAL SCORE of case III

	VAS SCORE	**WOMAC PAIN SCORE**	**WOMAC STIFFNESS SCORE**	**WOMAC FUNTIONALITY SCORE**	**WOMAC TOTAL SCORE**
'0' day	8	14	5	46	65
1st month	5	9	4	33	46
3rd month	3	8	2	26	36
6th month	2	4	1	16	21

PERCENTAGE (%) OF IMPROVEMENT: **67.69%**

GRADE OF RESULT: **FAIR.**

CASE N0 - 16

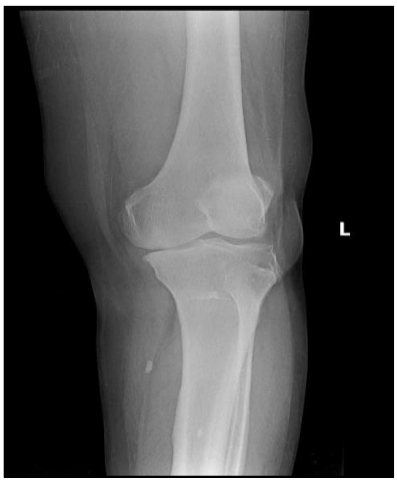
Age: 70 years

Sex: Female

UHID : 598394

Diagnosis: Osteoarthritis of Left Knee Grade-II

Date of Inflitraion: 05-07-2018



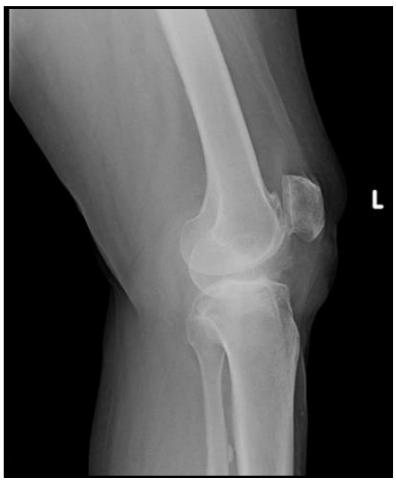


Table 33: VAS and WOMAC TOTAL SCORE of case IV

	VAS SCORE	WOMAC PAIN SCORE	WOMAC STIFFNESS SCORE	WOMAC FUNTIONALITY SCORE	WOMAC TOTAL SCORE
'0' day	7	15	3	54	72
1st month	5	12	2	49	63
3rd month	4	11	1	39	51
6th month	3	10	0	40	50

PERCENTAGE (%) OF IMPROVEMENT: **30.56%**

GRADE OF RESULT: **POOR.**

DISCUSSION

Articular cartilage lesions and degeneration are difficult to treat and present a challenge for orthopaedic surgeons because of the distinctive structure and function of hyaline cartilage and its inherent low healing potential.

This prospective observational study was performed to know the effectiveness of the PRP in 60 early osteoarthritis knee joints. Single autologous PRP injection was given. The efficacy of Platelet rich plasma in reducing pain, stiffness and physical function were assessed pre-injection and post-injection period on first month, third month and sixth month using WOMAC & VAS scores.

Age distribution: In this study the average age documented was 57.87±11.15 years which was comparable to findings of studies conducted by**,** Rayegani et al.[82], in 2014 and Raeissadat et al.[26], in 2015.

Table 34: Comparison of age distribution.

AUTHORS	YEAR	MEAN AGE
Patel et al.[19]	2013	53.11 ± 11.55
Rayegani et al.[82]	2014	58.07 ± 8.95
Raeissadat et al.[26]	2015	56.85 ± 9.13
Kavadar et al.[10]	2015	53.6 ± 6.7
Smith et al.[29]	2016	50.06 ± 9.35
Gormeli et al.[83]	2017	53.8 ± 13.4
IN PRESENT STUDY	2019	57.87 ± 11.15

.

Sex distribution: The male:female ratio in this study is 24:36. Most authors have documented female preponderance.

Table 35: Comparison of sex distribution.

AUTHORS	YEAR	SEX DISTRIBUTION (MALE: FEMALE)
Cerza et al.[84]	2012	25:35
Patel et al.[19]	2013	11:16
Raeissadat et al.[26]	2015	8:69
Gormeli et al.[83]	2017	16:23
IN PRESENT STUDY	2019	24:36

Knee Joint Side distribution: In our study Right knee joint is most commonly involved with 63.3% than that of left knee joint 36.7%, similar to studies done by Cerza et al.[84], in 2012 and patel et al.[19], in 2013.

Table 36: Comparison of knee joint side distribution.

AUTHORS	YEAR	KNEE JOINT SIDE DISTRIBUTION	
		RIGHT	LEFT
Cerza et al.[84]	2012	91	29
Patel et al.[19]	2013	78	78
IN PRESENT STUDY	2019	38	22

In this study, all the patients have shown decrease in their mean VAS scores. The mean VAS score at baseline was 7.08 ± 0.79 and the decrease in mean VAS score continued up to six months follow-up that is 2.78 ± 1.22 (P value <0.001) similar to the studies done by Patel et al.[19], in 2013 and Kavadar et al.[10], in 2015 and Çaliş et al.[85], in 2015 as shown in table below.

Table 37: Comparison of Mean VAS scores.

AUTHORS	YEAR	MEAN VAS at Baseline	MEAN VAS At six months
Patel et al.[19]	2013	4.5 ± 0.613	2.16 ± 1.543
Kavadar et al.[10]	2015	8.4 ± 1.2	4.5 ± 1.2
Çaliş et al.[27]	2015	8.1 ± 2.1	4.4 ± 2.9
IN PRESENT STUDY	2019	7.08 ± 0.79	2.78 ± 1.22

In this study, all the patients have shown decrease in the WOMAC score at final follow-up. Their mean WOMAC pain at baseline was 14.53±2.36 and the decrease in mean WOMAC pain continued up to six months follow-up that is 4.68±2.67 (P value <0.001) similar to the studies done by Patel et al.[19], in 2013, Fawzy et al.[31], in 2017 and Çaliş et al.[27], in 2015 & others as shown in table below.

Table 38: Comparison of Mean WOMAC PAIN scores.

AUTHORS	YEAR	WOMAC PAIN SCORE at Baseline	WOMAC PAIN SCORE at six months
Patel et al.[19]	2013	10.17 ± 3.82	5.00
Kavadar et al.[10]	2015	17.9 ± 0.5	16.9 ± 0.4
Çaliş et al.[27]	2015	16.6 ± 3.1	12.5± 4.6
Raeissadat et al.[26]	2015	8.46 ± 4.17	4.03 (3.36)
Fawzy et al.[31]	2017	14.3 ± 0.2	8.1 ± 0.6
IN PRESENT STUDY	2019	14.53 ± 2.36	4.68 ± 2.67

The WOMAC stiffness at baseline was 4.70±1.15 and the decrease in mean WOMAC stiffness continued up to six months follow-up that is 1.37±0.94 (P value <0.001) similar to the studies done by Patel et al.[19], in 2013, Çaliş et al.[27], in 2015 and Fawzy et al.[31], in 2017 & others as shown in table below.

Table 39: Comparison of Mean WOMAC STIFFNESS scores.

AUTHORS	YEAR	WOMAC STIFFNESS SCORE at Baseline	WOMAC STIFFNESS SCORE at six months
Patel et al.[19]	2013	3.06 ± 2.08	2.10
Kavadar et al.[10]	2015	6.5 ± 0.1	6.1 ± 0.2
Çaliş et al.[27]	2015	5.8 ± 2.4	4.6 ± 2.0
Raeissadat et al.[26]	2015	2.2 ± 1.76	1.19 ± 1.4
Fawzy et al.[31]	2017	3.1 ± 0.1	1.2 ± 0.5
IN PRESENT STUDY	2019	4.70 ± 1.15c	1.37 ± 0.94

The mean WOMAC Functionality at baseline was 14.53±2.36 and the decrease in mean WOMAC Functionality continued up to six months follow-up that is 13.90±8.70 (P value <0.001) similar to the studies done by Patel et al.[19], in 2013, Raeissadat et al.[26], in 2015 and Fawzy et al.[31], in 2017 & others as shown in table below.

Table 40: Comparison of Mean WOMAC FUNCTIONALITY scores.

AUTHORS	YEAR	WOMAC FUNCTIOALITY SCORE at Baseline	WOMAC FUNCTIONALITY SCORE at six months
Patel et al.[19]	2013	36.12 ± 13.08	20.08
Kavadar et al.[10]	2015	67.0 ± 1.4	64.6 ± 1.4
Çaliş et al.[27]	2015	8.9 ± 11.0	45.1 ± 13.5
Raeissadat et al.[26]	2015	28.91 ± 12.63	13.19 ± 10.39
Fawzy et al. [31]	2017	53.4 ± 1.2	39.1 ± 0.3
IN PRESENT STUDY	2019	46.98 ± 5.57	13.90±8.70

The mean WOMAC Total at baseline was 66.20 ± 7.63 and the decrease in mean WOMAC pain continued up to six months follow-up that is 19.95 ± 11.69 (P value <0.001) similar to the studies done by Patel et al[19]., in 2013, Raeissadat et al[26]., in 2015 and Fawzy et al[31]., in 2017 & others as shown in table below.

Tableb 41: Comparison of Mean WOMAC TOTAL scores.

AUTHORS	YEAR	WOMAC TOTAL SCORE at Baseline	WOMAC TOTAL SCORE at six months
Patel et al.[19]	2013	49.56±17.83	27.18
Kavadar et al.[10]	2015	91.4±2.0	87.6±1.9
Çaliş et al.[27]	2015	81.5±14.5	62.2±18.5
Raeissadat et al.[26]	2015	39.5±17.06	18.44±14.35
Fawzy et al.[31]	2017	70.8±1.5	48.4±1.4
IN PRESENT STUDY	2019	66.20±7.63	19.95±11.69

The improvement in mean VAS AND WOMAC scores in our patients could be explained by the fact that injected platelets might have acted at different levels and were stimulating the chondral anabolism or slowing the catabolic process.

There is a significant difference observed in Grade I and Grade II mean VAS scores. The mean VAS score in Grade I reduced from baseline (6.78±0.67) to final follow-up (2.17±0.89) compared to Grade II which reduced from baseline (7.27±0.80) to final follow-up 3.16±1.26 with significant change in P value.

There is a significant difference observed in Grade I and Grade II mean WOMAC TOTAL scores. The mean WOMAC TOTAL score in Grade I reduced from baseline (62.35±4.68) to final follow-up (14.22±4.26) compared to Grade II which reduced from baseline (68.59±8.16) to final follow-up (23.51±13.38) with significant change in P value.

As we have given a working classification to assess the results, 6 (10%) joints have shown excellent results, 29(48.3%) joints have shown good results, 18(30%) joints have shown fair results and 7(11.7%) joints have shown poor results, among excellent results 5(27%) were Grade I and one (2.7%) Patient Grade II.

COMPLICATIONS

Immediate post infiltration, few patients have complained of pain, but no local or systemic complications noted during our study. Sandeep Patel et al[19], in 2013, in their study have documented some systemic adverse effects but not lasting more than 30 minutes. Kon et al[86]. in 2010 and Sanchez et al[87]. in 2007 have reported some injection pain.

LIMITATIONS

The limitations of this study are short term follow-up period, small sample size, no control group. However, further studies on a larger population and longer follow up is recommended. Radiographic follow-up investigation methods such as magnetic resonance imaging may be considered for evaluating cartilage regeneration (if any) in subsequent research efforts.

CONCLUSION

Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability. It is a common, debilitating disease which is associated with a large social and economic burden, in addition to the physical and psychological sequelae it often manifests in the affected individual.

As of now, there are less treatment options available for patients with mild to moderate arthritis. Most of the approaches are palliative and address the symptoms rather than influencing the biochemical environment of the joint or the disease process.

Even though few studies suggest the use of multiple injections of PRP for early OA, but we observed that our results from usage of single PRP injection are comparable with them. We also observed that younger the patient and less severe the grade, better the results.

We can safely conclude that autologous PRP injection in early Osteoarthritis (Grade I and Grade II) does give relief from pain, stiffness and improves functionality without any major side effects and can be recommended as a viable modality of treatment.

We finally conclude that PRP is easy and convenient to extract, and processing is relatively simple and short, easy handling and offers multiple GFs at relatively inexpensive cost. Above all, its use is safe, and the results are easily reproducible with no or minimal complications.

SUMMARY

PRP is a relatively new treatment for early osteoarthritic knee joints with increasing number of studies showing promising results.

This is a prospective, observational, time bound study done on 60 Ahlback's radiological grade I and grade II osteoarthritic knee joints. Patients were selected in the outpatient and inpatient department of orthopaedics.

5 ml of autologous PRP prepared with single spinning technique at 1500 RPM for 15 minutes in the centrifuge machine in the blood bank.Total amount of sample infiltrated was 5 ml, into each knee joint under aseptic conditions in operation theatre.

Each patient was evaluated with VAS and WOMAC scoring on '0' day, 1 month ,3 month and six months. On assessing the results, there is a significant improvement in VAS & WOMAC score of all the patients with sustained results throughout the follow-up period of 6 months, which was confirmed by significant change of p value.

Better results were seen in grade I knee joints compared to grade II knee joints, with statistically significant difference in p value.

There were no long term local systemic complications noted through the course of the study except acute pain at the site of inject for 10-15 minutes immediately after the infiltration.

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ANNEXURE-I

PROFORMA

NAME: CASE NO:

AGE: UHID NO:

SEX: DOB:

ADDRESS: DATE:

MOBILE NO:

CHIEF COMPLAINT:

HISTORY OF PRESENTING ILLNESS:

PAST HISTORY:

FAMILY HISTORY:

GENRERAL PHYSICAL EXAMINATION:

VITAL SIGNS: SYSTEMIC EXAMINATION:

BP CVS

PR CNS

RR RS

TEMP P/A

LOCAL EXAMINATION:

INSPECTION:

PALPATION:

ROM:

X RAY FEATURES OF KNEE: Rt:

Lt:

AHLBACK RADIOLOGICAL GRADING:

OTHER INVESTIGATION:

CBC:

PLATELET COUNTS:

DIAGNOSIS:

WOMAC SCORE

	WOMAC PAIN	**WOMAC STIFFNESS**	**WOMAC FUNCTIONALITY**	**WOMAC TOTAL**
AT PRESENTATION				
1st FOLOW UP (1 month)				
2nd FOLLOW UP (3rd month)				
3rd FOLLOWUP (6th month)				
TOTAL				

VAS SCORE

AT PRESENTATION	
1st FOLOW UP (1 month)	
2nd FOLLOW UP (3rd month)	
3rd FOLLOWUP (6th month)	

ASSESSMENT OF RESULT:

Comments	
Principal Investigator Dr RAMMANOHAR SUREPALLY	Signature
Chief Investigator Dr NAGAKUMAR J. S	Signature

ANNEXURE - II

PATIENT INFORMATION SHEET

STUDY TITLE:

Effect of platelet rich plasma in osteoarthritis knee a short term follow up.

CHIEF RESEARCHER/ PG GUIDE'S NAME: Dr. NAGAKUMAR J S

PRINCIPAL INVESTIGATOR: Dr. RAMMANOHAR SUREPALLY

I, Dr RAMMANOHAR SUREPALLY, post-graduate student in Department of Orthopaedics at Sri Devaraj Urs Medical College. I will be conducting a study titled "A study of Effectiveness of platelet rich plasma in the treatment of mild to moderate osteoarthritis of knee joint" for my dissertation under the guidance of Dr. Nagakumar J.S, Professor, in Department of Orthopaedics. In this study, we will assess effect of intra articular injection of autologous platelet rich plasma of 5ml in patients presenting with mild to moderate degree of osteoarthritis of knee joint by assessing improvement in pain, functional outcome using WOMAC and VAS score's before the start of study and after injecting 1 month and 3 and 6^{th} month.

You will undergo X-ray of Knee routine investigations as part of procedure. You will be admitted and intra articular injection of autologous platelet rich plasma 5 ml given under monitoring. You will not be paid any financial compensation for participating in this research project.

All your personal data will be kept confidential and will be used only for research purpose by this institution. You are free to participate in the study. You can also withdraw from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution

Name and Signature of the Principal Investigator

Date:

ANNEXURE-III

INFORMED CONSENT FORM

STUDY TITLE:

Effect of platelet rich plasma in osteoarthritis of knee a short term follow up.

CHIEF RESEARCHER/ PG GUIDE'S NAME: Dr. NAGAKUMAR J S

PRINCIPAL INVESTIGATOR: Dr. RAMMANOHAR SUREPALLY.

NAME OF THE SUBJECT:

AGE :

GENDER :

a. I have been informed in my own language that this study includes x-ray of Knee, routine investigations and Intra articular injection of autologous plate rich plasma as part of procedure. I have been explained thoroughly and understand its complication and possible side effects.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that i

may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature/thumb impression

Signature of the witness: Date:

1)

2)

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

KEY TO MASTER CHART

S.NO	Serial number
M	Male
F	Female
UHID.No	Unique hospital identification number
LT	Left
RT	Right
WOMAC	Western ontario and mcmaster universities osteoarthrits index
VAS	Visual Analogue Score.

MASTER CHART

S.NO	AGE	GENDER	UHID NO	KNEE JOINT SIDE	GRADE OF OA	VAS				WOMAC SCORE (MAX 20)				WOMAC SCORE (MAX 8)				WOMAC SCORE (MAX 68)				WOMAC SCORE (MAX 96)				%OF IMPROVEMENT	GRADE OF RESULT
						0'DAY	1 MONTH	3 MONTH	6 MONTH	0'DAY	1 MONTH	3 MONTH	6 MONTH	0'DAY	1 MONTH	3 MONTH	6 MONTH	0 DAY	1 MONTH	3 MONTH	6 MONTH	0'DAY	1 MONTH	3 MONTH	6 MONTH		
1	56	F	513595	RT	II	8	6	4	2	18	11	11	9	7	5	5	3	58	41	35	24	83	57	51	36	56.63	FAIR
2	50	F	525500	LT	II	8	6	4	3	17	11	10	7	6	4	3	2	57	39	24	10	80	54	37	19	76.25	GOOD
3	60	M	538463	LT	II	7	5	4	4	14	11	6	2	3	2	0	0	48	33	21	9	65	46	27	11	83.08	GOOD
4	45	F	420791	RT	I	7	6	5	3	13	11	6	4	5	4	3	1	44	36	25	10	62	51	34	15	75.81	GOOD
5	48	F	536643	LT	I	7	5	4	3	13	9	7	4	4	2	2	1	41	31	17	12	58	42	26	17	70.69	GOOD
6	40	M	543212	RT	I	7	5	4	3	13	9	6	2	4	3	2	1	43	30	19	13	60	42	27	16	73.33	GOOD
7	49	M	543805	RT	II	8	6	4	3	17	12	9	5	5	3	2	1	47	34	20	12	69	49	31	18	73.91	GOOD
8	50	F	547888	RT	I	6	5	4	2	13	9	6	4	5	4	3	2	45	34	20	12	63	47	29	18	71.43	GOOD
9	62	M	557453	RT	II	6	5	4	3	13	9	6	4	4	4	2	2	43	31	18	9	60	44	26	15	75.00	GOOD
10	43	F	559124	RT	I	6	5	4	3	13	9	7	3	5	4	2	1	46	32	16	10	64	45	25	14	78.13	GOOD
11	60	F	584019	RT	II	7	5	4	2	14	9	7	5	4	3	3	1	45	29	22	13	63	41	32	19	69.84	FAIR
12	54	F	509631	RT	II	6	4	3	3	12	11	6	5	4	3	2	1	42	36	24	16	58	50	32	22	62.07	FAIR
13	65	F	586737	RT	II	6	4	3	2	12	10	6	4	6	4	2	2	47	34	24	14	65	48	32	20	69.23	FAIR
14	56	M	585690	RT	II	6	5	4	3	13	10	7	3	5	3	3	1	46	34	25	16	64	47	35	20	68.75	FAIR
15	60	M	592528	RT	II	7	5	4	3	13	10	8	4	4	3	3	1	44	31	24	14	61	44	35	19	68.85	FAIR
16	70	F	598394	LT	II	7	5	5	4	15	12	11	10	3	2	1	0	54	49	39	40	72	63	51	50	30.56	POOR
17	45	F	606281	LT	I	6	5	4	4	12	9	5	4	4	4	2	2	41	31	21	12	57	44	28	18	68.42	FAIR
18	65	M	569768	LT	II	7	5	4	3	18	13	8	6	5	4	3	2	47	34	25	14	70	51	36	22	68.57	FAIR
19	65	M	607388	RT	II	8	6	5	4	18	13	8	7	5	4	3	2	48	34	22	14	71	51	33	23	67.61	FAIR
20	56	M	319767	LT	I	8	5	3	2	14	9	8	4	5	4	2	1	46	33	26	16	65	46	36	21	67.69	FAIR
21	41	M	375735	RT	I	6	4	2	1	13	9	7	4	4	3	2	1	44	34	22	14	61	46	31	19	68.85	FAIR
22	60	M	608569	RT	II	7	5	3	2	17	13	9	7	5	4	2	2	46	35	24	14	68	52	35	23	66.18	FAIR
23	58	F	550962	RT	II	8	6	4	2	13	11	8	6	4	4	2	2	46	39	26	17	63	54	36	25	60.32	FAIR
24	65	M	634815	LT	I	6	5	3	2	15	12	8	5	2	2	2	1	36	32	21	14	53	46	31	20	62.26	FAIR
25	65	M	634736	RT	I	8	6	5	4	15	11	7	4	4	3	2	1	40	28	15	10	59	42	24	15	74.58	GOOD
26	55	F	549730	RT	I	6	5	4	2	17	13	9	7	6	4	3	2	38	32	25	13	61	49	37	22	63.93	FAIR
27	72	F	650831	RT	II	6	5	4	4	16	15	10	8	4	3	2	1	42	40	38	36	62	58	50	45	27.42	POOR
28	63	F	674367	RT	II	7	6	5	3	13	8	6	2	5	3	2	1	51	35	24	14	69	46	32	17	75.36	GOOD
29	55	F	656525	LT	II	8	6	5	3	15	11	7	4	5	3	2	1	41	29	21	8	61	43	30	13	78.69	GOOD
30	46	F	660403	RT	II	6	5	4	2	10	7	3	1	5	3	2	1	42	30	19	5	57	40	24	7	87.72	EXCELLENT
31	55	F	549418	RT	II	8	6	5	3	16	11	6	3	4	3	2	1	59	41	26	9	79	55	34	13	83.54	GOOD

MASTER CHART

32	44	M	635793	LT	I	6	5	4	2	13	9	5	2	3	2	1	0	45	31	19	11	61	42	25	13	78.69	GOOD
33	88	F	541607	RT	II	8	7	7	6	15	14	13	11	5	5	4	4	49	46	39	35	69	65	56	50	27.54	POOR
34	43	F	658777	RT	II	8	6	4	2	14	10	5	2	6	4	3	1	50	37	22	9	70	51	30	12	82.86	GOOD
35	55	F	549730	LT	II	6	4	3	2	7	5	4	3	1	1	1	0	36	26	21	7	44	32	26	10	77.27	GOOD
36	50	M	692880	LT	I	6	4	2	1	11	9	6	3	3	3	2	1	40	28	16	9	54	40	24	13	75.93	GOOD
37	72	M	678803	RT	II	6	4	3	2	14	10	5	3	5	3	2	1	45	28	16	6	64	41	23	10	84.38	GOOD
38	50	M	692303	LT	II	8	6	4	2	15	10	6	3	5	3	2	1	49	32	19	7	69	45	27	11	84.06	GOOD
39	50	M	692880	LT	II	8	6	4	2	12	9	7	3	7	5	3	2	53	34	21	12	72	48	31	17	76.39	GOOD
40	43	F	692034	RT	I	7	5	4	2	14	10	5	3	5	3	2	1	44	28	11	4	63	41	18	8	87.30	EXCELLENT
41	43	F	692803	RT	I	7	5	3	2	13	8	5	3	5	3	2	1	43	27	16	5	61	38	23	9	85.25	EXCELLENT
42	66	M	698267	LT	II	7	5	4	2	17	12	8	3	4	3	2	1	62	38	25	11	83	53	35	15	81.93	GOOD
43	64	M	701057	RT	II	8	7	6	6	18	17	13	12	6	5	4	3	57	51	46	39	81	73	63	54	33.33	POOR
44	50	M	701053	RT	I	7	5	3	1	11	8	5	2	3	2	2	1	49	34	21	8	63	44	28	11	82.54	GOOD
45	85	F	699671	RT	II	8	7	6	6	19	17	14	12	6	5	5	4	54	50	43	38	79	72	62	54	31.65	POOR
46	85	F	699671	LT	II	8	7	6	6	18	15	13	11	5	5	4	4	53	43	36	29	76	63	53	44	42.11	POOR
47	65	M	645390	RT	II	7	5	3	3	16	13	9	6	5	4	3	2	54	44	30	17	75	61	42	25	66.67	FAIR
48	65	M	645390	LT	II	8	6	4	3	16	11	10	7	5	4	3	2	50	39	30	15	70	54	43	24	65.71	FAIR
49	73	F	706258	RT	II	8	6	5	4	15	11	7	5	5	4	3	2	51	38	24	16	71	53	34	23	67.61	FAIR
50	73	F	706258	LT	II	8	6	5	3	15	11	9	7	5	4	3	2	46	29	20	10	66	44	32	19	71.21	GOOD
51	62	F	703688	RT	I	7	5	3	2	13	9	8	3	5	4	2	2	47	36	23	11	65	49	33	16	75.38	GOOD
52	62	F	703688	LT	II	7	5	3	2	18	13	8	3	5	4	3	1	53	40	23	10	76	57	34	14	81.58	GOOD
53	60	F	706368	RT	I	7	5	3	1	18	13	8	3	5	3	2	0	48	33	25	8	71	49	35	11	84.51	GOOD
54	66	F	711660	LT	II	8	6	5	3	18	13	8	3	5	3	2	1	49	34	21	8	72	50	31	12	83.33	GOOD
55	55	F	651907	RT	I	8	6	5	2	16	12	8	3	5	3	2	0	51	36	21	7	72	51	31	10	86.11	EXCELLENT
56	55	F	651907	LT	I	7	5	3	1	14	10	7	2	4	3	1	0	48	32	20	7	66	45	28	9	86.36	EXCELLENT
57	46	F	722188	RT	I	7	6	5	2	16	11	7	3	6	4	3	1	47	32	21	9	69	47	31	13	81.16	GOOD
58	46	F	722188	LT	I	7	5	4	2	13	9	6	2	4	3	1	0	44	29	17	5	61	41	24	7	88.52	EXCELLENT
59	72	M	679803	RT	II	7	6	5	5	15	13	12	8	8	4	3	2	38	35	34	29	61	52	49	39	36.07	POOR
60	50	F	729983	RT	I	7	5	4	3	13	9	6	3	5	3	2	1	47	32	21	8	65	44	29	12	81.54	GOOD