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# EVALUATION OF EFFICACY AND SAFETY OF THERAPEUTIC INTERVENTIONS IN KNEE OSTEOARTHRITIS: A COMPARATIVE STUDY ASSESSING CLINICAL, FUNCTIONAL, RADIOLOGICAL, AND BIOCHEMICAL OUTCOMES

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**ABSTRACT** Osteoarthritis is a progressive degenerative joint disease associated with pain, inflammation, and functional disability. This study evaluated the efficacy and safety of therapeutic interventions in patients with knee osteoarthritis.A prospective observational comparative study was conducted at Hamdard Institute of Medical Sciences and Research from April 2024 to June 2025 involving 100 patients with Kellgren–Lawrence grade I–II knee OA. Clinical, functional, and biochemical parameters including VAS, WOMAC, KOOS, SF-36, ROM, hs-CRP, ESR, calcium, vitamin $D_3$, and muscle strength were assessed at baseline, 1, 3, and 6 months. Significant improvements were observed in all assessed parameters over 6 months ($p < 0.001$). VAS scores decreased from $8.56 \pm 1.10$ to $3.17 \pm 1.55$, while WOMAC scores improved from $86.84 \pm 9.19$ to $41.17 \pm 12.62$. ROM increased from $109.58 \pm 10.24°$ to $135.92 \pm 5.95°$. KOOS and SF-36 scores improved significantly, indicating better functional status and quality of life. Inflammatory markers (hs-CRP and ESR) decreased, while calcium and vitamin $D_3$ levels improved. Quadriceps and hamstring strength also increased progressively.The therapeutic intervention significantly improved pain, joint function, muscle strength, and inflammatory status in knee OA patients, suggesting its potential as an effective management strategy.

**KEYWORDS :** Knee Osteoarthritis; WOMAC; VAS; KOOS; Inflammation; ROM; Quality of Life.

## INTRODUCTION

Osteoarthritis (OA) is a highly prevalent, chronic degenerative joint disorder and a leading cause of pain and disability worldwide, particularly among middle-aged and elderly populations.[1] It is characterized by progressive deterioration of articular cartilage, subchondral bone remodeling, synovial inflammation, and osteophyte formation, ultimately resulting in joint stiffness, reduced mobility, and impaired quality of life.[1] [3] Knee osteoarthritis, in particular, represents the most common form of the disease, significantly contributing to functional limitation and socioeconomic burden.[2] Epidemiological studies indicate that the global prevalence of OA is steadily increasing, with projections suggesting a substantial rise in disease burden due to aging populations, sedentary lifestyles, and increasing obesity rates.[4] [7]

The pathogenesis of osteoarthritis is multifactorial, involving biomechanical, biochemical, and genetic factors. Aging, obesity, joint injury, malalignment, and metabolic disorders are among the primary risk factors that accelerate cartilage degradation and impair its regenerative capacity.[4] [5] As cartilage lacks vascularization and has limited intrinsic healing potential, damage tends to accumulate over time, leading to progressive joint degeneration.[1] The knee joint, being weight-bearing and frequently subjected to mechanical stress, is particularly vulnerable to these degenerative changes.[8]

Despite significant advances in understanding OA pathophysiology, the disease remains incurable, and current management strategies primarily focus on symptomatic relief rather than disease modification.[6] Conventional therapeutic approaches include nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, lifestyle modification, and intra-articular injections such as corticosteroids and hyaluronic acid.[2] [3] While these interventions may alleviate pain and improve joint function, their effects are often temporary and associated with potential adverse effects, especially with long-term use.[3] Consequently, there is a growing need for safer, more effective, and sustainable treatment options that not only relieve symptoms but also target the underlying mechanisms of disease progression.[6]

Radiographic assessment plays a crucial role in the diagnosis and grading of OA, with the Kellgren–Lawrence grading system being the most widely accepted method for evaluating disease severity.[10] [12] However, radiological methods have limitations in detecting early disease changes. Increasing attention has therefore been directed toward biochemical and molecular markers involved in cartilage degradation and inflammation. Matrix metalloproteinase-13 (MMP-13), a key enzyme involved in extracellular matrix breakdown, has been shown to degrade proteoglycans and collagen components of cartilage.[13] [14]Additionally, inflammatory cytokines play a central role in OA pathogenesis by stimulating catabolic pathways and promoting cartilage destruction.[6]

In recent years, alternative and adjunctive therapeutic strategies have gained attention for improving joint health and patient outcomes. However, variability in clinical response and limitations in long-term effectiveness continue to challenge optimal disease management.[3] In this context, the present study aims to evaluate the efficacy and safety of therapeutic interventions compared with the standard of care in improving symptoms of knee osteoarthritis. The study further seeks to assess improvements in knee joint range of motion (ROM), evaluate pain reduction using the Visual Analogue Scale, and determine functional outcomes using validated indices such as the WOMAC Osteoarthritis Index, KOOS, and SF-36. Additionally, radiological changes, including joint space width on standard knee radiographs, will be examined. Secondary outcomes include evaluation of rescue medication use, analysis of inflammatory markers (ESR, CRP, CBC, RBS), and documentation of adverse events.

## MATERIALS AND METHODS

This prospective observational comparative study was conducted at the Hamdard Institute of Medical Sciences and Research and its associated Hakeem Abdul Hameed Centenary Hospital, New Delhi, from April 2024 to June 2025. Patients aged 40–55 years with radiologically confirmed Kellgren–Lawrence grade I–II knee osteoarthritis attending the Orthopaedics OPD/IPD were included. Exclusion criteria comprised prior knee fractures, malignancy-related joint pathology, deformity, previous knee surgery or injury, and active infection.

Participants were allocated into two groups: Group A received

standard care (paracetamol as needed, calcium, vitamin $D_3$, and physiotherapy), while Group B received an additional intervention alongside standard care for 3 months.

Assessments were performed at baseline, 1, 3, and 6 months, including knee range of motion (ROM), pain (VAS), and functional scores (WOMAC, KOOS, SF-36). Radiological evaluation included standing AP and lateral knee radiographs to measure joint space width. Laboratory parameters (CBC, ESR, CRP, RBS) were assessed pre- and post-treatment. Adverse events were recorded throughout.

Ethical approval was obtained from the Institutional Ethics Committee, and written informed consent was secured from all participants. Statistical analysis was performed using IBM SPSS Statistics, with significance set at $p < 0.05$.

## RESULTS

### Demographic Characteristics

A total of 100 participants were included in the study. The majority were female (n = 70; 70.0%), while males constituted 30.0% (n = 30). This distribution indicates a predominance of female patients, consistent with the higher prevalence of osteoarthritis among women reported in existing literature (Table 1).

### Anthropometric Outcomes (BMI)

At baseline, the mean body mass index (BMI) of the Standard Group was 30.27 kg/m², indicating obesity. A gradual decline in BMI was observed over the follow-up period, reaching 30.06 kg/m² at 1 month, 29.65 kg/m² at 3 months, and 29.27 kg/m² at 6 months. By the end of the study, participants transitioned from the obese to the overweight category, reflecting modest but consistent improvement in anthropometric status(Table 1).

### Clinical Outcomes

The mean osteoarthritis (OA) grade showed a gradual reduction from 2.95 ± 0.845 to 2.78 ± 0.91, 2.44 ± 1.028, and 2.47 ± 1.123 at 1, 3, and 6 months, respectively, indicating mild improvement in disease severity. Knee range of motion (ROM) improved progressively from 109.58 ± 10.24° to 114.69 ± 9.90°, 124.92 ± 9.23°, and 135.92 ± 5.95° over the same time points, reflecting substantial recovery in joint mobility.

The WOMAC Osteoarthritis Index score decreased from 86.84 ± 9.19 to 79.63 ± 9.67, 65.20 ± 10.63, and 41.17 ± 12.62 at 1, 3, and 6 months, respectively, indicating marked improvement in pain, stiffness, and physical function. Pain scores, assessed using the Visual Analogue Scale, declined from 8.56 ± 1.10 to 7.59 ± 1.17, 5.64 ± 1.31, and 3.17 ± 1.55 over the study period, demonstrating clinically meaningful pain relief. Similarly, KOOS scores improved from 33.41 ± 8.00 to 38.54 ± 8.69, 48.79 ± 10.07, and 67.16 ± 13.45, while SF-36 scores increased from 48.39 ± 7.19 to 53.23 ± 8.28, 62.91 ± 10.47, and 79.51 ± 11.25 at 1, 3, and 6 months, respectively, indicating enhanced functional status and overall quality of life.

### Biochemical Parameters

High-sensitivity C-reactive protein (hs-CRP) levels declined from 4.79 ± 1.26 mg/L to 4.36 ± 1.27, 3.51 ± 1.30, and 2.57 ± 1.35 mg/L at 1, 3, and 6 months, respectively, indicating a reduction in systemic inflammation. Uric acid levels decreased from 8.17 ± 0.86 mg/dL to 7.73 ± 0.90, 6.85 ± 0.98, and 5.96 ± 1.07 mg/dL over the same time points, reaching the normal range by the end of the study. Calcium levels improved from 8.24 ± 0.70 mg/dL to 8.47 ± 0.74, 8.92 ± 0.83, and 9.38 ± 0.88 mg/dL, remaining within normal limits throughout follow-up. Vitamin $D_3$ levels increased steadily from 17.29 ± 4.46 ng/mL to 20.39 ± 4.74, 26.60 ± 5.31, and 31.85 ± 5.70 ng/mL, reaching the lower normal range at 6 months. Erythrocyte sedimentation rate (ESR) decreased from 34.81 ± 8.73 mm/hr to 31.36 ± 8.30, 24.45 ± 7.44, and 15.83 ± 5.90 mm/hr, indicating normalization by the end of the study period (Table 2).

### Muscle Strength

Quadriceps muscle strength (MMT) improved from 3.74 ± 0.87 to 3.90 ± 0.72, 4.17 ± 0.92, and 4.41 ± 0.81 at 1, 3, and 6 months, respectively. Similarly, hamstring strength increased from 3.84 ± 0.76 to 3.88 ± 0.89, 4.22 ± 0.77, and 4.51 ± 0.67 over the same time points, reflecting progressive recovery of muscle function (Table 2).

### 3.1 Evolution of Clinical and Biochemical Markers During Follow-Up

In the present study, 100 patients were evaluated for 13 clinical, functional, and biochemical parameters at baseline, 1, 3, and 6 months. Repeated-measures ANOVA demonstrated statistically significant improvements across all parameters over the study period (all $p < 0.001$).

Pain intensity, assessed using the Visual Analogue Scale, decreased markedly from 8.56 ± 1.10 to 3.17 ± 1.55 at 6 months, representing an approximate 63% reduction ($p < 0.001$). Functional disability, measured by the WOMAC Osteoarthritis Index, improved substantially from 86.84 ± 9.19 to 41.17 ± 12.62 ($p < 0.001$).

Patient-reported outcomes showed consistent improvement, with KOOS increasing from 33.41 ± 8.00 to 67.16 ± 13.45 and SF-36 from 48.39 ± 7.19 to 79.51 ± 11.25 (both $p < 0.001$). Knee range of motion (ROM) improved significantly from 109.58 ± 10.24° to 135.92 ± 5.95° ($p < 0.001$), while OA grade showed a modest but significant reduction from 2.95 ± 0.84 to 2.47 ± 1.12 ($p < 0.001$).

Biochemical parameters also demonstrated significant improvement. High-sensitivity C-reactive protein (hs-CRP) decreased from 4.79 ± 1.26 to 2.57 ± 1.35 mg/L, and erythrocyte sedimentation rate (ESR) declined from 34.81 ± 8.73 to 15.83 ± 5.90 mm/hr (both $p < 0.001$). Serum uric acid levels reduced from 8.17 ± 0.86 to 5.96 ± 1.07 mg/dL ($p < 0.001$), while calcium and vitamin $D_3$ levels improved from 8.24 ± 0.70 to 9.38 ± 0.88 mg/dL and 17.29 ± 4.46 to 31.85 ± 5.70 ng/mL, respectively (both $p < 0.001$).

Muscle strength, assessed using manual muscle testing, improved in both the quadriceps (3.74 ± 0.87 to 4.41 ± 0.81) and hamstrings (3.84 ± 0.76 to 4.51 ± 0.67) ($p < 0.001$), with the most pronounced improvements observed between 1 and 3 months (Table 3) (Figure 1a – 1m).

## DISCUSSION

The incidence of osteoarthritis (OA) continues to rise globally, largely driven by aging populations, increasing obesity, and sedentary lifestyles. The present study evaluated clinical, functional, and biochemical outcomes over a 6-month period and demonstrated significant improvements across all assessed parameters, suggesting the effectiveness of the therapeutic approach in managing knee OA.

In the present study, a higher proportion of female participants (70%) was observed, which is consistent with existing literature indicating a greater prevalence of OA among women.[15] Hormonal changes, particularly post-menopausal estrogen decline, along with biomechanical and genetic factors, may contribute to this increased susceptibility. Additionally, the baseline body mass index (BMI) indicated obesity, with gradual reduction over the study period. This supports the well-established association between obesity and OA progression, where excess body weight increases mechanical stress on joints and promotes systemic inflammation.[16]

Significant improvements were observed in clinical outcomes, including pain, functional status, and joint mobility. Pain reduction, as assessed using the Visual Analogue Scale, showed a marked decline over time, indicating effective symptomatic relief. Similarly, functional disability measured using the WOMAC Osteoarthritis Index improved substantially, reflecting better joint function and reduced stiffness. These findings are consistent with previous studies demonstrating that effective interventions can significantly improve pain and function in OA patients.[17]

Biochemical parameters demonstrated a consistent reduction in inflammatory markers. The decline in hs-CRP and ESR levels suggests attenuation of systemic inflammation, which plays a central role in OA pathogenesis. These findings are in agreement with studies by Hanada et al., who reported elevated inflammatory markers in OA patients.[18] The reduction in serum uric acid levels observed in this study may further indicate decreased inflammatory activation, potentially linked to reduced stimulation of the NLRP3 inflammasome pathway, as suggested by Denoble et al..[19]

Additionally, improvements in calcium and vitamin $D_3$ levels were observed, which may contribute to better bone metabolism and joint health. Previous studies, such as Li et al., have demonstrated an inverse relationship between calcium levels and OA severity.[20] Vitamin D deficiency has also been associated with increased pain and functional impairment in OA patients.[21]

Muscle strength, particularly of the quadriceps and hamstrings, improved significantly during the study period. Strengthening of periarticular muscles is essential for joint stabilization, reducing mechanical load, and improving functional outcomes. These findings are consistent with rehabilitation-based studies showing that muscle strengthening significantly improves OA symptoms.[22]

Overall, the findings of the present study suggest that a combined therapeutic approach can lead to significant improvements in pain, function, inflammation, and muscle strength in patients with knee OA. However, certain limitations should be considered. The study had a relatively moderate sample size and a follow-up duration limited to six months, which may not fully capture long-term outcomes. Future studies with larger populations and longer follow-up are needed to validate these findings and explore long-term benefits.

## CONCLUSION

In the present study, significant improvements were observed in clinical, functional, and biochemical parameters among patients with knee osteoarthritis over the 6-month follow-up period. Reductions in pain, as assessed by the Visual Analogue Scale, along with improvements in functional outcomes measured using the WOMAC Osteoarthritis Index, KOOS, and SF-36, indicate substantial enhancement in patient quality of life.

Additionally, the observed increase in knee range of motion (ROM) and improvement in muscle strength reflect better joint function and physical performance. Biochemical findings, including reductions in hs-CRP, ESR, and uric acid levels, along with improvements in calcium and vitamin $D_3$ levels, suggest a decrease in systemic inflammation and improved metabolic status.

Overall, the findings of this study support the effectiveness of the therapeutic intervention in managing knee osteoarthritis by addressing both symptomatic relief and underlying inflammatory processes. However, given the relatively limited sample size and duration of follow-up, further large-scale and long-term studies are warranted to confirm these findings and establish sustained clinical benefits.

**Table 1: Demographic and Anthropometric Characteristics of the Study Population (Standard Group)**

| | |
|---|---|
| Total Participants (N) | N 100 |
| Female, n (%) | 70 (70.0%) |
| Male, n (%) | 30 (30.0%) |
| BMI (kg/m²) | |
| Baseline | 30.27 |
| 1 Month | 30.06 |
| 3 Months | 29.65 |
| 6 Months | 29.27 |

N = total number of participants; n = number of patients; % = percentage of total sample; BMI = Body Mass Index; kg/m² = kilograms per square meter.

**Table 2: Clinical, Functional, and Biochemical Outcomes at Different Follow-Up Time Points (Standard Group)**

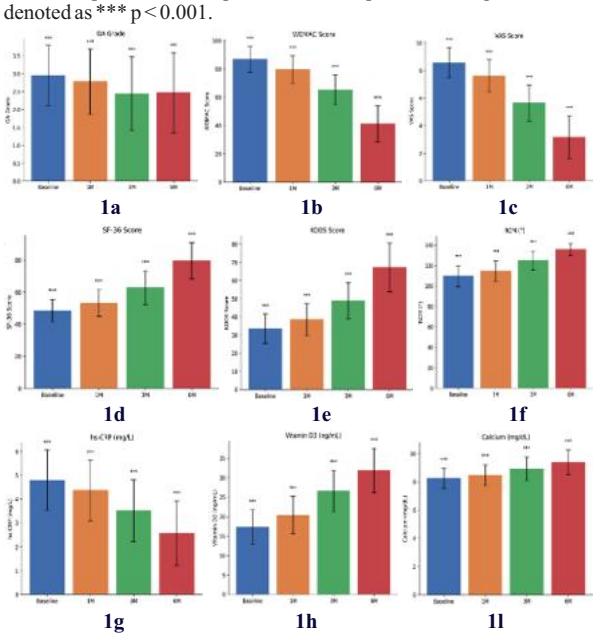
| Parameter | Baseline | 1 Month | 3 Months | 6 Months |
|---|---|---|---|---|
| OA Grade | 2.95 ± 0.845 | 2.78 ± 0.91 | 2.44 ± 1.028 | 2.47 ± 1.123 |
| ROM (°) | 109.58 ± 10.24 | 114.69 ± 9.9 | 124.92 ± 9.23 | 135.92 ± 5.95 |
| WOMAC Score | 86.84 ± 9.19 | 79.63 ± 9.67 | 65.20 ± 10.63 | 41.17 ± 12.62 |
| VAS Score | 8.56 ± 1.10 | 7.59 ± 1.17 | 5.64 ± 1.31 | 3.17 ± 1.55 |
| KOOS Score | 33.41 ± 8.00 | 38.54 ± 8.69 | 48.79 ± 10.07 | 67.16 ± 13.45 |
| SF-36 Score | 48.39 ± 7.19 | 53.23 ± 8.28 | 62.91 ± 10.47 | 79.51 ± 11.25 |
| hs-CRP (mg/L) | 4.79 ± 1.26 | 4.36 ± 1.27 | 3.51 ± 1.30 | 2.57 ± 1.35 |
| Uric Acid (mg/dL) | 8.17 ± 0.86 | 7.73 ± 0.90 | 6.85 ± 0.98 | 5.96 ± 1.07 |
| Calcium (mg/dL) | 8.24 ± 0.70 | 8.47 ± 0.74 | 8.92 ± 0.83 | 9.38 ± 0.88 |
| Vitamin $D_3$ (ng/mL) | 17.29 ± 4.46 | 20.39 ± 4.74 | 26.60 ± 5.31 | 31.85 ± 5.70 |
| ESR (mm/hr) | 34.81 ± 8.73 | 31.36 ± 8.30 | 24.45 ± 7.44 | 15.83 ± 5.90 |
| Quadriceps MMT | 3.74 ± 0.87 | 3.90 ± 0.72 | 4.17 ± 0.92 | 4.41 ± 0.81 |
| Hamstring MMT | 3.84 ± 0.76 | 3.88 ± 0.89 | 4.22 ± 0.77 | 4.51 ± 0.67 |

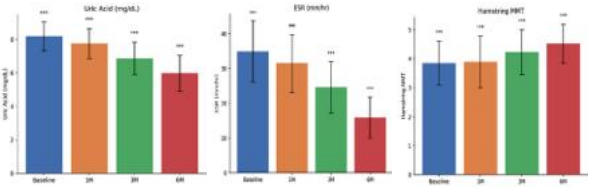
Values are expressed as mean ± standard deviation; OA = Osteoarthritis; ROM = Range of Motion; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = Visual Analogue Scale; KOOS = Knee Injury and Osteoarthritis Outcome Score; SF-36 = Short Form-36 Health Survey; hs-CRP = high-sensitivity C-reactive protein; ESR = Erythrocyte Sedimentation Rate; MMT = Manual Muscle Testing.

**Table 3: Baseline and Follow-up Values of Clinical, Functional, Biochemical, and Muscle Strength Parameters in Study Subjects**

| Parameter | Baseline (Mean ± SD) | 1 Month (Mean ± SD) | 3 Months (Mean ± SD) | 6 Months (Mean ± SD) | p-value | Signi-ficance |
|---|---|---|---|---|---|---|
| OA Grade | 2.95 ± 0.84 | 2.78 ± 0.91 | 2.44 ± 1.03 | 2.47 ± 1.12 | <0.001 | *** |
| ROM (°) | 109.58 ± 10.24 | 114.69 ± 9.90 | 124.92 ± 9.23 | 135.92 ± 5.95 | <0.001 | *** |
| WOMAC Score | 86.84 ± 9.19 | 79.63 ± 9.67 | 65.20 ± 10.63 | 41.17 ± 12.62 | <0.001 | *** |
| VAS Score | 8.56 ± 1.10 | 7.59 ± 1.17 | 5.64 ± 1.31 | 3.17 ± 1.55 | <0.001 | *** |
| KOOS Score | 33.41 ± 8.00 | 38.54 ± 8.69 | 48.79 ± 10.07 | 67.16 ± 13.45 | <0.001 | *** |
| SF-36 Score | 48.39 ± 7.19 | 53.23 ± 8.28 | 62.91 ± 10.47 | 79.51 ± 11.25 | <0.001 | *** |
| hs-CRP (mg/L) | 4.79 ± 1.26 | 4.36 ± 1.27 | 3.51 ± 1.30 | 2.57 ± 1.35 | <0.001 | *** |
| Uric Acid (mg/dL) | 8.17 ± 0.86 | 7.73 ± 0.90 | 6.85 ± 0.98 | 5.96 ± 1.07 | <0.001 | *** |
| Calcium (mg/dL) | 8.24 ± 0.70 | 8.47 ± 0.74 | 8.92 ± 0.83 | 9.38 ± 0.88 | <0.001 | *** |
| Vitamin $D_3$ (ng/mL) | 17.29 ± 4.46 | 20.39 ± 4.74 | 26.60 ± 5.31 | 31.85 ± 5.70 | <0.001 | *** |
| ESR (mm/hr) | 34.81 ± 8.73 | 31.36 ± 8.30 | 24.45 ± 7.44 | 15.83 ± 5.90 | <0.001 | *** |
| Quadriceps MMT | 3.74 ± 0.87 | 3.90 ± 0.72 | 4.17 ± 0.92 | 4.41 ± 0.81 | <0.001 | *** |
| Hamstring MMT | 3.84 ± 0.76 | 3.88 ± 0.89 | 4.22 ± 0.77 | 4.51 ± 0.67 | <0.001 | *** |

This section presents the longitudinal changes in all outcome parameters across four time points (baseline, 1 month, 3 months, and 6 months). Data are expressed as mean ± standard deviation. Statistical significance was determined using one-way repeated-measures ANOVA; p-values are reported for each parameter. Significance is denoted as *** $p < 0.001$.



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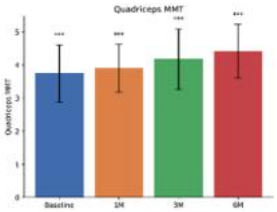


1m

**Figure 1a – 1m: Longitudinal Changes in Clinical, Functional, Biochemical, and Muscle Strength Parameters in Patients with Knee Osteoarthritis Over A 6-month Intervention Period. Data are Presented as Mean ± Standard Deviation at Four Time Points: Baseline, 1 Month, 3 Months, and 6 Months (n = 100). All Parameters Demonstrated Statistically Significant Changes Over Time ($p < 0.001$), As Determined by One-way Repeated-measures ANOVA. OA = Osteoarthritis; ROM = Range of Motion; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; VAS = Visual Analogue Scale; KOOS = Knee Injury and Osteoarthritis Outcome Score; SF-36 = 36-Item Short Form Health Survey; hs-CRP = High-sensitivity C-reactive Protein; ESR = Erythrocyte Sedimentation Rate; MMT = Manual Muscle Testing; Vit $D_3$ = Vitamin $D_3$. ***$p < 0.001$.**

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