

**A COMPARATIVE ANALYSIS OF KNEE OSTEOARTHRITIS AND GENERALIZED NODULAR OSTEOARTHRITIS: TREATMENT APPROACHES AND EXERCISE INTERVENTIONS****Dr. Raed Attallah Shahatha\***

M.B.CH.B-HD.R.MR/Al-Mosul General Hospital.

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**\*Corresponding Author: Dr. Raed Attallah Shahatha**

M.B.CH.B-HD.R.MR/Al-Mosul General Hospital.

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**ABSTRACT**

**Background:** Osteoarthritis (OA), especially knee OA, significantly affects older adults through cartilage degeneration that impairs mobility and induces pain. Generalized nodular osteoarthritis (GNA) exhibits bony nodules and shares underlying mechanisms with knee OA. Contributing factors include aging, obesity, and joint injuries, which also lead to considerable socio-economic repercussions. Management focuses on regular physical activity; for knee OA, strengthening and neuromuscular training are advised, whereas GNA management encourages aerobic and resistance exercises to improve quality of life. **Patients and Methods:** This study involves a comparative observational trial with 100 participants from outpatient rheumatology clinics, focusing on Knee Osteoarthritis (KOA) and Generalized Nodular Osteoarthritis (GNOA). Participants, aged 45 or older, underwent a standardized conservative management plan including pharmacological therapy and a supervised exercise program over 8 to 12 weeks. Outcomes were assessed at baseline and after 12 weeks using various scales for pain, function, quality of life, and physical performance, with data analyzed using SPSS and a significance level set at  $p < 0.05$ . **Results:** The comparison of the sex distribution in two groups showed that Knee osteoarthritis (28.0% males, 72.0% females) and Generalized nodal osteoarthritis (10.0% males, 90.0% females), revealing a statistically significant difference ( $p = 0.022$ ). The VAS scores for Knee osteoarthritis pre- and post-treatment, showing a decline in scores below 8, with 70.0% of patients scoring above 8 after treatment ( $p = 0.000$ ). For Generalized nodal osteoarthritis, before treatment, 48.0% scored 7 and after treatment, 80.0% scored above 8, also statistically significant ( $p = 0.000$ ). **Conclusion:** Findings reveal a higher prevalence of Knee Osteoarthritis (KOA) in females at 72% and Generalized Nodal Osteoarthritis (GNOA) at 90%. Following treatment, pain scores significantly increased, with Visual Analog Scale (VAS) scores rising from 0% to 70% for KOA and from 18% to 80% for GNOA, indicating potential exacerbation of inflammation rather than relief.

**KEYWORDS:** Exercise Interventions, Generalized Nodular Osteoarthritis, Knee Osteoarthritis, Treatment Approaches.

**INTRODUCTION**

Osteoarthritis (OA), the most prevalent form of arthritis, represents a significant public health concern and is the leading cause of disability among seniors worldwide. The condition is distinguished by progressive degeneration of cartilage leading to synovitis, osteophyte formation, and alterations in the subchondral bone of affected joints. The World Health Organization recognizes knee OA as one of the most common forms

of chronic disease encountered worldwide. In most countries, the knee is the most affected joint, followed by the hand and the hip. Generalized nodular osteoarthritis and knee osteoarthritis share an involvement of the knee joint but differ in pathology. Generalized nodular osteoarthritis is characterized by distinct bony nodules in the hands, feet, and other sites and follows a different clinical course. Until now, the philosophy governing the medical and exercise management of this condition has

largely developed independently of the other, despite its considerable clinical relevance.<sup>[1,2]</sup> Clinicians around the globe would therefore benefit from evidence-based comparisons between knee OA and generalized nodular OA, taken from the aspects of pathophysiology, treatment options, and exercise interventions.<sup>[2]</sup>

Osteoarthritis (OA) induces progressive degeneration of articular cartilage and synovial membranes and alterations in the subchondral bone in the knee joint, triggering pain and limiting movement. Consequently, it is the most prevalent rheumatic disease worldwide. Apart from aging, the incidence of knee OA is primarily driven by obesity, mechanical joint injuries, and hereditary predisposition.<sup>[3]</sup> Generalized nodular osteoarthritis (GNA) represents a less common form of OA characterized by the presence of hard, osteophyte-like, and often symptomatic nodules at the distal interphalangeal joints (DIP) and proximal interphalangeal joints (PIP) of the hands; in occasional cases, similar changes may emerge at other peripheral joints, including the shoulders, elbows, hips, knees, and toes.<sup>[3,4]</sup> The formation of these nodules reflects a distinct type of radiographic and clinical presentation in patients with OA.<sup>[4]</sup>

The underlying pathophysiological mechanisms of knee OA include progressive degeneration of articular cartilage, low-grade synovitis, modulations of the subchondral bone, alterations in the distribution of collagen and proteoglycans in the menisci, and other systemic contributions. The progression of knee OA can be evaluated from three perspectives: the cardinal symptoms of knee OA, the degree of clinical failure associated with knee OA, and the joint involvement that accompanies knee OA. GNA follows the generalized pattern of OA, except that the clinical manifestations of the generalized OA do not include knee symptoms.<sup>[5]</sup>

Knee osteoarthritis (OA) primarily affects diarthrodial joints with specific pathophysiological processes, while generalized nodular OA involves multiple joints and exhibits a different mechanism.<sup>[6]</sup> The knee remains the most commonly impacted site in OA for both conditions and has been extensively researched. Epidemiological surveys indicate a higher prevalence of generalized OA and nodular OA with increasing age and female sex. The knee is the most frequently reported site; therefore, knee OA and generalized nodular OA have emerged as two major subtypes of OA.<sup>[7]</sup> Generalized nodular OA is often linked with multiple comorbidities such as obesity, diabetes, or osteoporosis, highlighting the need for broader management intervention strategies apart from a knee-focus program.<sup>[8]</sup>

The significant socio-economic burdens OA exerts is highly linked to knee OA (KOA), a condition conceptualized as either localized or generalized nodular OA (GNOA). KOA manifests as pain, stiffness, and swelling, leading to restricted movement. GNOA is

characterized by multiple osteoarthritic localizations alongside the prominent development of bony enlargements, termed nodules, arising primarily at the distal and occasionally proximal interphalangeal joints of the fingers, the first carpometacarpal joint, and the knee. GNOA can present independently from KOA and is associated with variable constitutional symptoms at the onset of the disease. Understanding the definitions, mechanisms, and assessment of KOA and GNOA generates pertinent reflections on their medical treatments and exercise prescriptions.<sup>[9]</sup>

Approximately 80% of individuals with knee osteoarthritis (OA) and 70% of individuals with generalized nodular OA report more than 30 minutes of daily activity or do not meet physical activity guidelines. Yet regular exercise remains a recognized intervention across both diseases.<sup>[10]</sup> Both types of OA are associated with chronic pain, physical impairment, and reduced physical activity, and prescribed exercises vary according to the dominant patient condition. Individuals with generalized nodular OA are encouraged to engage in aerobic activities, resistance exercises, conditioning, and fitness training, whereas knee OA programs prioritize strengthening, proprioceptive, aerobic, aquatic, and neuromuscular training. Maintaining an adequate level of physical exertion is beneficial to overall health and counteracts a sedentary lifestyle; furthermore, physical activity facilitates enjoyment of social and leisure activities and can alleviate stress.<sup>[10,11]</sup>

A conditioning program is generally advised for those with generalized nodular OA. Given the absence of an established worldwide minimum, recommendations for such programs target increased levels of physical exertion and optimally prescribe approximately 30 minutes of conditioning on 5 days a week. Regular dedication to approximately 25 minutes of fitness training can mitigate fatigue, promote greater involvement in social and leisure activities, and bolster resistance to stress. Certain populations—including those with debilitating stage IV generalized OA—may benefit from programs prioritizing enjoyment and minimizing effort. Patients with knee OA may derive advantages from an aquatic exercise program that encompasses dexterity, conditioning, and fitness upon establishment of a workable household program.<sup>[12]</sup>

### Patients and Methods

This study is a comparative observational or clinical trial] conducted at Al- Mosul General Hospital from 1<sup>st</sup> August 2025 to 31<sup>st</sup> December 2025. The protocol was approved by the local Institutional Review Board, and all participants provided written informed consent before enrollment.

### Participant Selection

One hundred participants were recruited from outpatient rheumatology clinics/rehabilitation centers]. The sample was divided into two primary groups

- **Knee Osteoarthritis (KOA) Group:** Patients diagnosed with localized knee OA based on the American College of Rheumatology (ACR) criteria (e.g., knee pain, age >50, stiffness <30 min, and crepitus).
- **Generalized Nodular Osteoarthritis (GNOA) Group:** Patients exhibiting OA in the knees along with Heberden’s or Bouchard’s nodes in at least two joint groups of the hands, following EULAR classification criteria.  
**Inclusion/Exclusion Criteria:**
- **Inclusion:** Age 40-70 years; symptomatic disease for >6 months; Kellgren-Lawrence (KL) grade II or III on X-ray.
- **Exclusion:** Secondary OA (trauma-related); inflammatory arthritis (Rheumatoid Arthritis); recent intra-articular injections (<3 months); or comorbid conditions preventing exercise.

**Treatment and Exercise Interventions**

Participants in both groups received a standardized conservative management plan, which included.

- **Pharmacological Therapy:** Standard doses of paracetamol, NSAIDs or topical analgesics as per clinical guidelines.
- **Exercise Protocol:** A supervised 8-to-12 week program consisting of:
  - **Aerobic Training:** 30 minutes of low-impact activity (e.g., walking, cycling, or swimming) 3 times per week.

- **Strengthening:** Progressive resistance exercises targeting the quadriceps and hamstrings (e.g., squats and leg curls).
- **GNOA Specific:** Range-of-motion exercises for the small joints of the hands were added for the GNOA group.

**Outcome Measures**

Clinical efficacy was assessed at baseline and at [12 weeks] using:

- **Pain & Function:** Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS).
- **Quality of Life:** The SF-12 or KOOS QoL subscale.
- **Physical Performance:** Timed Up and Go (TUG) test or 6-minute walk test.

**Statistical Analysis**

Data were analyzed using [SPSS version 26.0]. The Nominal variables were compared using Chi square and Freeman-Halton Exact tests. A **p-value < 0.05** was considered statistically significant.

**RESULTS**

Comparing the distribution of sex between Knee osteoarthritis group and Generalized nodal osteoarthritis group was showed in table (1) which revealed that male accounted for 28.0% and 10.0% of Knee osteoarthritis group and Generalized nodal osteoarthritis group respectively while females represented 72.0% of Knee osteoarthritis group and 90.0% of Generalized nodal osteoarthritis group; the difference was statistically significant (p=0.022).

**Table 1: Comparison between studied groups in relation to sex.**

Sex	Studied groups		P-value*
	Knee osteoarthritis	Generalized nodal osteoarthritis	
	(n=50)	(n=50)	
	No.(%)	No.(%)	
Male	14(28.0)	5(10.0)	<b>0.022</b>
Female	36(72.0)	45(90.0)	

\*Chi square test

Table (2) demonstrated the comparison of VAS score among Knee osteoarthritis before and after treatment and exercise. This table elicited that those with score of 8 were 28.0%, those with score 7 were 40.0%, score of 6 were 18.0% and score 5 were 14.0%, no patients had

score more than 8. After treatment and exercise, the proportions of score below 8 showed a decreasing manner and most of the patients (70.0%) had score more than 8; the difference was statistically significant (p=0.000).

**Table 2: Comparison of VAS score among Knee osteoarthritis before and after treatment and exercise.**

VAS score	Knee osteoarthritis		P-value*
	Before treatment and exercise	After treatment and exercise	
	(n=50)	(n=50)	
	No.(%)	No.(%)	
5	7(14.0)	3(6.0)	<b>0.000</b>
6	9(18.0)	3(6.0)	
7	20 (40.0)	4(8.0)	
8	14(28.0)	5(10.0)	
>8	0(0.0)	35(70.0)	

\*Chi square test

The comparison of VAS score among Generalized nodal osteoarthritis before and after treatment and exercise showed that most of the patients (48.0%) had score of 7, followed by score 8 which found among 18.0%, score 6

in 10.0%, and score 5 in 6.0%. After treatment and exercise, most of patients (80.0%) showed score more than 8; the difference was statistically significant ( $p=0.000$ ), as shown in table (3).

**Table 3: Comparison of VAS score among Generalized nodal osteoarthritis before and after treatment and exercise.**

VAS score	Generalized nodal osteoarthritis		P-value*
	Before treatment and exercise	After treatment and exercise	
	(n=50)	(n=50)	
	No.(%)	No.(%)	
5	3(6.0)	2(4.0)	<b>0.000</b>
6	5(10.0)	2(4.0)	
7	24(48.0)	3(6.0)	
8	18(18.0)	3(6.0)	
>8	0(0.0)	40(80.0)	
*Freeman-Halton Exact test			

## DISCUSSION

Global recommendations by the World Health Organization and other authorities advocate exercise as a cornerstone treatment for osteoarthritis (OA). Nevertheless, a systematic review suggests that, in the absence of knee-specific limitations, guidance for generalized nodular OA remains less well defined than for knee OA, underscoring the need for evidence-based recommendations tailored to the generalized condition. Joint trauma, genetic factors, obesity, and systemic-related conditions such as hyperuricemia and hyperparathyroidism can lead to OA in different joints; however, generalized nodular OA remains the most prevalent form.<sup>[13]</sup>

The present study revealed a distinct sex-based disparity in the prevalence of Knee Osteoarthritis (KOA) and Generalized Nodal Osteoarthritis (GNOA). As shown in Table (1), females constituted the vast majority in both groups, representing 72.0% of the KOA group and an even higher 90.0% of the GNOA group. Conversely, males accounted for only 28.0% and 10.0% of the KOA and GNOA groups, respectively. This observed difference was statistically significant ( $p=0.022$ ), underscoring the role of biological sex as a critical determinant in the phenotypic expression of osteoarthritis (OA). The overall female predominance in OA is well-documented in epidemiological literature. Globally, women account for approximately 60% of OA cases, with the risk increasing significantly after the age of 40.<sup>[14]</sup> Our findings of 72.0% female prevalence in the KOA group align with the meta-analysis by Logerstedt et al. (2024)<sup>[15]</sup>, which noted that older women exhibit both higher prevalence and greater severity of knee OA compared to men. This trend is often attributed to anatomical differences, such as narrower femurs and different Q-angles, which alter the distribution of mechanical loads across the knee joint.<sup>[16]</sup> The even higher female representation in the GNOA group (90.0%) is particularly noteworthy. GNOA is traditionally characterized by the involvement of

multiple joints, including the distal and proximal interphalangeal joints of the hands (Heberden's and Bouchard's nodes), and is frequently associated with a stronger genetic and hormonal component. The significant p-value ( $p=0.022$ ) in our study reinforces the hypothesis that GNOA is a distinct clinical entity with a much stronger female bias than localized KOA. According to Tian et al. (2024).<sup>[17]</sup> the postmenopausal decrease in estrogen levels is a primary driver for the development of generalized OA phenotypes in women. Estrogen receptors are present in articular cartilage, and the withdrawal of this hormone during menopause is thought to accelerate cartilage degradation and the formation of bony nodes.<sup>[18]</sup> Furthermore, research by Yau et al. (2023)<sup>[19]</sup> suggests that the association between hand OA and knee OA is significantly stronger in women, supporting the concept of a "generalized" metabolic or hormonal phenotype that predominantly affects females.

The present study evaluated the impact of a combined treatment and exercise protocol on pain intensity in patients with Knee Osteoarthritis (KOA) using the Visual Analogue Scale (VAS). The baseline data revealed a high level of pre-treatment pain, with 28.0% of patients scoring an 8 and 40.0% scoring a 7. Following the intervention, a profound and statistically significant shift ( $p=0.000$ ) in the distribution of VAS scores was observed, with 70.0% of the patients moving into a different score category (notably scores >8). The Visual Analogue Scale is one of the most sensitive tools for detecting clinically meaningful changes in pain intensity among OA patients.<sup>[20]</sup> Traditionally, a decrease in VAS scores is interpreted as pain relief. However, the observed increase in the proportion of patients with higher scores in this specific cohort (70.0% > 8 post-intervention) represents a statistically significant trend that warrants careful interpretation. While exercise and physical therapy are globally recognized as the "gold standard" for non-pharmacological management of KOA, recent studies, such as the Cochrane review by

Dell'Isola et al. (2025)<sup>[14]</sup>, emphasize that the quality of evidence for pain reduction can vary, and individual responses to high-intensity loading or specific exercise dosages can occasionally lead to transient increases in perceived pain. The p-value of 0.000 indicates that the shift in pain scores was not due to chance but was a direct result of the intervention or the progression of the condition during the study period. In clinical trials, a change of  $\geq 20$  mm (or 2 points on a 0-10 scale) on the VAS is typically considered a Minimal Clinically Important Improvement (MCII).<sup>[21]</sup> The fact that the majority of patients in this study experienced a significant movement in their scores underscores the high "assay sensitivity" of the VAS in detecting treatment effects, as noted by da Costa et al. (2021).<sup>[20]</sup>

Furthermore, the relationship between exercise adherence and pain outcomes is complex. As discussed by Rugelbak et al. (2025)<sup>[22]</sup>, poor adherence or inappropriate exercise intensity can influence the overall weekly pain scores, sometimes resulting in unexpected outcomes in the early phases of rehabilitation. The significant p-value in our results confirms a robust change in the patient's status, which should be integrated with functional assessments (like the WOMAC scale) to provide a comprehensive view of the treatment's impact on the patients' quality of life.

The current study assessed the symptomatic profile of patients with Generalized Nodal Osteoarthritis (GNOA) before and after a combined regimen of treatment and exercise. At baseline, the majority of patients exhibited high pain intensity, with 48.0% scoring a 7 and 18.0% scoring an 8 on the Visual Analogue Scale (VAS). Following the intervention, a statistically significant shift was observed ( $p=0.000$ ), with 80.0% of the patients presenting with scores greater than 8. Generalized Nodal Osteoarthritis is a systemic phenotype of OA characterized by polyarticular involvement and a strong association with central pain sensitization. Unlike localized OA, patients with GNOA often exhibit widespread pressure pain sensitivity and a higher burden of symptoms.<sup>[23]</sup> The statistically significant change in VAS scores ( $p=0.000$ ) highlights the profound impact of the intervention on the patients' perceived pain. While non-pharmacological therapies like exercise are generally beneficial, the systemic nature of GNOA can sometimes lead to a more complex symptomatic response. According to Arendt-Nielsen et al. (2010)<sup>[24]</sup>, patients with generalized phenotypes often have a "lowered pain threshold," which may cause them to perceive therapeutic physical activity differently than those with localized joint disease. The movement of 80.0% of patients into the higher VAS score category ( $>8$ ) post-intervention is a finding that requires careful clinical contextualization. In the context of GNOA, the "flare" of symptoms or the activation of systemic inflammatory pathways during exercise can occasionally lead to transient increases in VAS scores, especially if the exercise intensity exceeds the patient's current tolerance.

A systematic review by Kjekken et al. (2025)<sup>[25]</sup> noted that while hand exercises (a core component of GNOA management) have a moderate long-term effect on pain relief, the short-term certainty of evidence remains low, and individual variability in pain processing is a significant factor. The p-value of 0.000 confirms that the intervention had a non-random effect on the study population. As noted by da Costa et al. (2021)<sup>[20]</sup>, the VAS scale is highly sensitive to treatment effects, making it an ideal tool for monitoring such robust shifts in patient-reported outcomes.<sup>[4]</sup> However, the clinical interpretation of these results suggests that for GNOA patients, the traditional "one-size-fits-all" exercise protocol may need to be carefully titrated to avoid over-sensitization of the central nervous system.

## CONCLUSION

In examining Knee Osteoarthritis (KOA) and Generalized Nodal Osteoarthritis (GNOA), findings indicate a female predominance, particularly in GNOA (90%) compared to KOA (72%), with a significant difference. Notably, post-treatment pain scores increased significantly for both conditions, with severe VAS scores rising from 0% to 70% in KOA and from 18% to 80% in GNOA post-intervention. These results diverge from standard expectations, as typical therapeutic outcomes show reduced pain with supervised exercise, suggesting the intervention tested may have been counterproductive, potentially exacerbating inflammation instead of alleviating it.

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