

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا  
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ  
الْحَكِيمُ

صدق الله العظيم

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# **Advances in the Understanding of Osteoarthritis**

**ESSAY**

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**BY**

**Mahmood Hadi Nassi**

*M.B.Ch.B.*

*Al-Mustansiriya University*

*Baghdad, Iraq*

**Supervised by**

**Professor Dr. Mayada Ali Abdalla**

*Assistant Prof. of Rheumatology and Rehabilitation*

*Faculty of Medicine*

*Cairo University*

**Dr. Dina Abbas Effat**

*Lecturer of Rheumatology and Rehabilitation*

*Faculty of Medicine*

*Cairo University*

**Faculty of Medicine**

**Cairo University**

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# المستجد في معرفة مرض التهاب العظمي المفصلي

رسالة توطئة للحصول علي درجة  
الماجستير في الروماتيزم والتأهيل

مقدمة من الطبيب

**محمود هادي نصي**

بكالوريوس طب وجراحة عامة

الجامعة المستنصرية

بغداد - العراق

تحت اشراف

**الأستاذة الدكتورة / ميادة علي عبد الله**

استاذ مساعد الروماتيزم والتأهيل

كلية طب

جامعة القاهرة

**الدكتورة / دينا عباس محمد**

مدرس الروماتيزم والتأهيل

كلية طب

جامعة القاهرة

كلية الطب

جامعة القاهرة

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# ABSTRACT

Osteoarthritis (OA) is the most common joint disorder worldwide. It is a chronic degenerative disorder characterized by cartilage loss. OA prevalence is high, and it is a major cause of disability. Numerous factors have been associated with an increased risk for the development of OA; these include systemic factors such as genetics, age and gender as well as local mechanical factors such as joint injury, joint deformity and muscle weakness. Therapies for OA have been directed mostly toward the alleviation of signs and symptoms of the disease, predominantly manifested by pain. Evaluating therapeutic efficacy has largely focused on improvement in pain and joint function.

Management of OA, the most common form of arthritis, involves a combination of nonpharmacological, pharmacological, and surgical options in advanced cases. As the populations of developed nations age over the next few decades, the need for better understanding of osteoarthritis and for improved therapeutic alternatives will continue to grow.

**Key Words** : osteoarthritis , etiopathogenesis , non-pharmacological options , DMOADs .

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## LIST OF ABBREVIATIONS

Abbreviation	Meaning
<b>ACCP</b>	Anticyclic citrullinated peptide.
<b>ACR</b>	American College of Rheumatology.
<b>ACT</b>	Autologous chondrocytes transplantation.
<b>ACU</b>	Avocado/Soybean unsaponifiables.
<b>ADAPT</b>	Diet and activity promotion trial.
<b>AGG</b>	Aggrecan.
<b>ALK5</b>	Activin-like kinase 5.
<b>AQE</b>	Aquatic exercise.
<b>AS</b>	Ankylosing spondylitis.
<b>ATP</b>	Adenosine triphosphate.
<b>AUSCAN</b>	Australian/Canadian osteoarthritis hand index.
<b>BLOKS</b>	Boston leeds osteoarthritis score.
<b>BMD</b>	Bone mineral density.
<b>BMI</b>	Body mass index.
<b>BML</b>	Bone marrow lesion.
<b>BMP</b>	Bone morphogenetic protein.
<b>BT</b>	Balneotherapy.
<b>CMC</b>	Carpometacarpal .
<b>COMP</b>	Cartilage oligomeric matrix protein.
<b>COX-2</b>	Cyclooxygenase -2.
<b>CPPD</b>	Calcium pyrophosphate dehydrate.
<b>CR</b>	Conventional radiography.
<b>CRP</b>	C-Reactive protein.
<b>CS</b>	Chondroitin sulfate.
<b>CT</b>	Computed tomography.
<b>CTX-II</b>	C-terminal cross linked telopeptide typeII collagen.
<b>DESS</b>	Coronal double echo steady state .
<b>DIP</b>	Distal interphalangeal .
<b>DISH</b>	Diffuse idiopathic skeletal hyperostosis.
<b>DJD</b>	Degenerative joint disease.
<b>DMOADs</b>	Disease modifying osteoarthritis drugs.
<b>DMSO</b>	Dimethylsulfoxide.
<b>E2</b>	Estrogen.
<b>ECM</b>	Extra cellular matrix.
<b>ECM</b>	Extracellular matrix.
<b>EOA</b>	Erosive osteoarthritis.
<b>ERT</b>	Estrogen replacement therapy.
<b>EULAR</b>	European league against rheumatism.

<b>Abbreviation</b>	<b>Meaning</b>
<b>FAOS</b>	The Foot and Ankle outcome score.
<b>FasL</b>	Fast ligand.
<b>FIHOA</b>	Functional index for hand osteoarthritis.
<b>FOS</b>	Facet osteoarthritis sign.
<b>FSE</b>	Fast spin echo.
<b>GAGPS</b>	Glycosaminoglycan polysulfuric acid.
<b>GI</b>	Gastrointestinal.
<b>GLU</b>	Glucosamine.
<b>HA</b>	Hyaluronic acid.
<b>HLA</b>	Human leukocyte antigen.
<b>HMG-COA</b>	Hydroxymethylglutaryl-Co enzyme.
<b>HOOS</b>	Hip disability and Osteoarthritis Outcome Score.
<b>HRQOL</b>	Health-related Quality of life.
<b>ICE</b>	Interleukin-1 converting enzyme.
<b>IDEA</b>	Intensive diet and exercise for Arthritis.
<b>IGF-1</b>	Insulin-like growth factor-I.
<b>IL-1</b>	Interleukin-1.
<b>IL-1Ra</b>	IL-1 receptor antagonist.
<b>ILsR</b>	Interleukin-1 soluble receptor.
<b>iNOS</b>	Inducible nitric oxide synthase.
<b>JCA</b>	Juvenile chronic polyarthritis.
<b>JSN</b>	Joint space narrowing.
<b>JSW</b>	Joint space width.
<b>KOOS</b>	Knee osteoarthritis outcome Score.
<b>LBE</b>	Land-based exercise.
<b>MCP</b>	Metacarpophalangeal.
<b>MCP-1</b>	Monocyte chemoattractant protein-1.
<b>MED</b>	Multiple epiphyseal dysplasia.
<b>MMP</b>	Matrix metalloproteinase.
<b>MRI</b>	Magnetic resonance imaging.
<b>MSM</b>	Methylsulfonyl methane.
<b>MSCs</b>	Mesenchymal stem cells.
<b>MTP</b>	Metatarsophalangeal.
<b>NFκB</b>	Nuclear factor-κB .
<b>NGF</b>	Nerve growth factor.
<b>NHANES</b>	National health and nutrition examination survey.
<b>NHP</b>	Nottingham health profile.
<b>NHS</b>	National health service.
<b>NO</b>	Nitric oxide.
<b>NPDS</b>	Pain and disability scale.



<b>Abbreviation</b>	<b>Meaning</b>
<b>OA</b>	Osteoarthritis.
<b>OARSI</b>	Osteoarthritis research society international.
<b>OASFs</b>	Osteoarthritis synovial fibroblasts.
<b>OI</b>	Ocular inflammation.
<b>PEMF</b>	Pulsed electromagnetic fields.
<b>PFP</b>	Passion fruit peel.
<b>PGE-2</b>	Prostaglandin E-2.
<b>PIP</b>	Proximal interphalangeal.
<b>PMNs</b>	Polymorphonuclear leukocyte
<b>RA</b>	Rheumatoid arthritis.
<b>RAGE</b>	Receptor for advanced glycation end products.
<b>RF</b>	Rheumatoid factor.
<b>ROS</b>	Reactive oxygen species.
<b>SAMe</b>	S-adenosyl methionine.
<b>SF</b>	Synovial fluid.
<b>SFs</b>	Synovial fibroblasts.
<b>sHLA</b>	Soluble isoforms HLA.
<b>SLCs</b>	Synovial lining cells.
<b>SNP</b>	Single nucleotide polymorphism.
<b>SOD</b>	Superoxide dismutase.
<b>SPGR</b>	Spoiled gradient-recalled echo.
<b>TENS</b>	Transcutaneous electrical nerve stimulation.
<b>TGF-<math>\beta</math></b>	Transforming growth factor- $\beta$ .
<b>THA</b>	Total hip arthroplasty.
<b>TIMP</b>	Tissue inhibitor of matrix metalloproteinase.
<b>TKA</b>	Knee-joint arthroplasty.
<b>TMJ</b>	Temporomandibular joint.
<b>TNF</b>	Tumor necrosis factor.
<b>TNF-Sr</b>	Tumor necrosis factor soluble receptor.
<b>VAS</b>	Visual analogue scale.
<b>VIL-10</b>	Viral interleukin -10.
<b>WOMAC</b>	Western ontario and McMaster universities.
<b>WORMS</b>	Whole-organ magnetic resonance imaging score.

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## **Introduction and Aim of the work**

Osteoarthritis (OA) is the most common articular disease worldwide; its high prevalence entails significant costs to society .Direct costs of osteoarthritis include clinician visits, medications, and surgical intervention,indirect cost is the time lost from work. As the populations of developed nations age over the next few decades, the need for better understanding of osteoarthritis and for improved therapeutic alternatives will continue to grow (*Lozada,2009*).

It is becoming increasingly apparent that the subchondral bone, periosteum, periarticular ligaments, periarticular muscle , synovium, and joint capsule are all richly innervated and are the likely source of nociception in osteoarthritis .In addition, it is apparent that local tissue alterations in the bone and meniscus and alignment of the lower extremity are important in terms of disease genesis (*Hunter ,2009*).

New diagnostic recommendations for knee osteoarthritis,have been published, one on risk factors :female sex, aging, overweight, joint injury, malalignment, joint laxity, occupational and recreational use, family history, and Heberden's nodes (bone overgrowth at the distal finger joints), and one on clinical diagnosis that focused on 3 symptoms: pain on use, short-lived morning stiffness, and functional limitation, and 3 signs : crepitus, restricted movement, and bony enlargement.The third recommendation called for plain radiography of the knees, with a weight bearing, semi-flexed view, plus a lateral and skyline view (*Zhang,2009*).

A group of patients show fast progression of the disease process leading to disability and ultimately joint replacement. Apart from symptom relief, no treatments have been identified that could eradicate the disease process. Therefore, there has been increasing attention devoted to the understanding of the mechanisms that are driving the disease process. The biology of the cartilage-subchondral bone unit has been highlighted as a key in osteoarthritis, and pathways that involve both cartilage and bone formation and turnover have become prime targets for modulation, and thus therapeutic intervention (*Luyten et al., 2008*).

Therefore the aim of this work is to demonstrate the advances in etiopathogenesis, clinical assessment and management of osteoarthritis.

## **Epidemiology and Etiopathogenesis**

### **EPIDEMIOLOGY**

Osteoarthritis is derived from the Greek word "osteo" meaning of the bone, "arthro" meaning joint, and "itis" meaning inflammation, although the "itis" of osteoarthritis is somewhat of a misnomer as inflammation is not a conspicuous feature.

By the age of 65, more than 80% of the population have radiographic changes consistent with osteoarthritis in at least one site (hands, feet, spine, knees, or hips), 40% complain of arthritic symptoms, and 10% report limitation in activity due to arthritis. Women, after the perimenopausal period, are more likely to develop osteoarthritis of the knees, hips, and hands than are men (*Issa and Sharma, 2006*).

The prevalence of OA (the frequency of the disease in the population at a given time), varies according to the definition of OA, the specific joints under study, and the characteristics of the study population. The prevalence of radiographic and symptomatic knee, hand, and hip OA has been estimated. The age-standardized prevalence of radiographic knee OA in adults over the age of 45 years was 19.2% among the participants in the Framingham Study (the prevalence of radiographic and symptomatic knee Osteoarthritis of independently living elderly in the early 1980s at which time they had been observed for over 35 years and many risk factors for Osteoarthritis had been ascertained. This study suggested that knee osteoarthritis increases in prevalence throughout the elderly years, more so in women than in men. Also, studies of risk factors have shown that obesity precedes and increases the risk of knee