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Review Paper

A review on risk factors and symptoms associated with arthritis

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ABSTRACT:
This review explores the risk factors and symptoms associated with arthritis, with a focus on osteoarthritis (OA), rheumatoid arthritis (RA), and gout. Arthritis is a multifaceted condition influenced by genetic, environmental, and lifestyle factors. The prevalence of arthritis increases with age, and women are more susceptible than men. Key risk factors include family history, obesity, joint injuries, infections, and smoking. Symptoms such as joint pain, stiffness, swelling, decreased range of motion, and fatigue significantly impact patients' quality of life. Early diagnosis and intervention are crucial to managing arthritis effectively and preventing severe joint damage. Present biological and clinical markers, including elevated CRP levels and the number of swollen and tender joints, play a vital role in early identification and management. This review underscores the importance of understanding the pathomechanisms and risk factors of arthritis to develop targeted therapies and improve patient outcomes.

Keywords: Arthritis, Epidemiology, Infection, Risk factor

INTRODUCTION:

Arthritis, derived from the Greek words “arthro,” meaning joint, and “itis,” meaning inflammation, is a broad term encompassing over 100 distinct conditions characterized by inflammation of the joints. This ailment has been recognized since ancient times, with evidence suggesting that it afflicted both Neanderthals and ancient Egyptians (Pahwa et al., 2020). Today, arthritis continues to be a prevalent and often debilitating condition, affecting millions of people worldwide and significantly impacting their quality of life.

One of the most common forms of arthritis is osteoarthritis (OA), also known as degenerative joint disease. OA primarily involves the breakdown of cartilage, the protective tissue that cushions the ends of bones within joints. This degradation leads to pain, stiffness, and decreased mobility, particularly in weight-bearing joints such as the knees, hips, and spine (Felson, 2004). The pathogenesis of OA is multifactorial, involving mechanical, genetic, and biochemical factors, and it is most frequently associated with aging and repetitive joint use (Hunter & Bierma-Zeinstra, 2019).

Rheumatoid arthritis (RA) is another prevalent form of arthritis but is distinguished from OA by its autoimmune nature. RA occurs when the body's immune system mistakenly attacks the synovium, the lining of the membranes surrounding the joints. This immune response leads to inflammation, pain, and potentially significant joint damage and deformity if left untreated (Smolen et al., 2018). RA is a systemic disease, meaning it can affect other parts of the body beyond the joints, including the skin, eyes, lungs, and cardiovascular system.

Inflammatory arthritis encompasses several other conditions, including psoriatic arthritis, ankylosing spondylitis, and gout. Each of these conditions has unique pathophysiological mechanisms and clinical presentations but shares the common feature of joint inflammation (McInnes & Schett, 2017). Psoriatic arthritis, for instance, is associated with the skin condition psoriasis and can cause joint pain, stiffness, and swelling. Ankylosing spondylitis primarily affects the spine and can lead to severe, chronic pain and stiffness in the back. Gout, caused by the deposition of urate crystals within the joint, typically presents with sudden and severe pain, redness, and swelling, often in the big toe (Dalbeth et al., 2016).

Diagnosing arthritis involves a combination of clinical evaluations, laboratory tests, and imaging studies. Clinical evaluations typically include a detailed patient history and physical examination to assess symptoms, joint function, and overall health. Laboratory tests may involve blood tests to identify markers of inflammation or autoimmunity, such as erythrocyte sedimentation

rate (ESR), C-reactive protein (CRP), and rheumatoid factor (RF) (Aletaha & Smolen, 2018). Imaging studies, including X-rays, MRI, and ultrasound, are utilized to visualize joint damage and inflammation, aiding in the accurate diagnosis and monitoring of arthritis progression (McQueen & Ostergaard, 2017).

Continued research into the pathophysiology of arthritis is crucial for developing targeted treatments and improving patient outcomes. Advances in understanding the genetic and molecular mechanisms underlying arthritis have paved the way for the development of new therapies and personalized treatment approaches (McInnes & Schett, 2017). Additionally, public health initiatives aimed at promoting early diagnosis and intervention, as well as patient education and self-management, are essential components of comprehensive arthritis care (Brady et al., 2019).

Understanding the risk factors and symptoms associated with arthritis is crucial for early detection, management, and prevention. This review explores the various risk factors and symptoms of the most common types of arthritis: Osteoarthritis (OA), Rheumatoid Arthritis (RA), and Gout.

In conclusion, arthritis is a complex and multifaceted condition that poses significant challenges to individuals and healthcare systems worldwide. By enhancing our understanding of its underlying mechanisms, improving diagnostic approaches, and developing more effective treatments, we can mitigate the impact of arthritis and improve the lives of those affected by this debilitating condition.

EPIDEMIOLOGY OF ARTHRITIS:

More than one-third of the American population shows signs of arthritis on imaging, and this figure is anticipated to rise as the average age of the population increases (Hazes JM et.al,.2011). Among the various types of arthritis, osteoarthritis is the most common. Between 19% and 30% of adults over 45 years old have knee osteoarthritis (Hart DJ, et. al,1993). while 27% have osteoarthritis in the hand, and another 27% in the hip (Heliövaara M. et. al,1993). It is projected that 40% of men and 47% of women will experience osteoarthritis in their lifetime, with the likelihood increasing to 60% for those with a body mass index (BMI) over 30 (Senthelal S. et al, 2023).

In 2020, it was estimated that 55.8 million people globally had gout, with an age-standardized prevalence of 659 per 100,000. This represents a 22.5% increase since 1990 (He, Q., Mok, et.al,.2023). The burden of gout is expected to continue rising, with projections suggesting a 55% increase in gout mortality by 2060 (Mattiuzzi, C., et al,.2019).

Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects millions of people worldwide. RA is more common in women, with a female-to-male prevalence ratio of 2.45. About 70% of people with RA are women, and 55% are older than 55 years (World Health Organization. 2023).

According to a study approximately 17.6 million people worldwide were living with rheumatoid arthritis (RA), with an age-standardized global prevalence rate of 208.8 cases per 100,000 population. This represents a 14.1% increase since 1990. RA was more prevalent among females, with a female-to-male prevalence ratio of 2.45. The age-standardized death rate in 2020 was 0.47 per 100,000 populations, accounting for about 38,300 global deaths, a 23.8% decrease since 1990. The disability-adjusted life year (DALY) count for RA in 2020 was 3.06 million, with an age-standardized DALY rate of 36.4 per 100,000 populations, and 76.4% of these DALYs were attributed to years lived with disability (YLDs). Smoking was responsible for 7.1% of RA-related DALYs. By 2050, it is projected that 31.7 million individuals will be living with RA globally. (Rachel J. Black et. al,.2020,)

The burden of RA is expected to continue rising, with projections suggesting that 31.7 million individuals will be living with RA worldwide by 2050 (ER England, et. al, 2024)

Septic arthritis is typically caused by bacterial seeding of an already arthritic joint via the hematogenous spread, most often from skin or urinary tract infection. Septic arthritis has a prevalence of 0.01% in the general population and 0.7% in patients with rheumatoid arthritis.

PATHOPHYSIOLOGY OF RHEUMATOID ARTHRITIS:

Rheumatoid arthritis (RA) is a complex autoimmune disease characterized by persistent synovial inflammation and progressive joint destruction. The pathophysiology of RA involves three key interacting pathological processes: chronic inflammation, hyperplasia of the synovium (pannus formation), and increased osteoclastogenic activity. Symptoms of rheumatoid arthritis are typically more severe than those of osteoarthritis. Rheumatoid arthritis is a systemic and chronic inflammatory state caused by an autoimmune response to an environmental trigger. The degradation of cartilage and, eventually, bone is preceded by endothelial cell activation and synovial cell hyperplasia. The pathology occurs following the aberrant production of inflammatory mediators (such as tumor necrosis alpha, interleukins 1, 6 and 8 and others following exposure to an antigenic pathogen (De Hair MJ, et.al.,2014).

The monosodium urate salts of gout precipitate as needle-shaped crystals. This crystallization is more likely to occur in cooler body parts and with acidic conditions. Destabilization of these deposited intraarticular uric acid crystals leads to IL-1 mediated inflammatory response leading to the typical acute gouty arthritis flare. The process is different in

pseudogout where the inorganic pyrophosphate from chondrocytes combines with calcium to form calcium pyrophosphate dihydrate. This crystal is deposited in joint spaces that have a predilection to osteoarthritic changes. Pseudogout crystal damage includes the fragmentation of bone and cartilage and the formation of osteophytes and subchondral cysts. Metabolic disorders such as hemochromatosis, hyperparathyroidism, or hypomagnesemia increase the likelihood of calcium pyrophosphate deposition (Struglics A. et.al,. 2015).

The hyperplasia of the synovium results in the formation of a pannus, an invasive tissue comprising fibroblast-like synoviocytes (FLS) and other cellular subpopulations. The pannus invades adjacent cartilage and bone, leading to their destruction. Matrix metalloproteinases (MMPs) produced by cells at the pannus-cartilage interface play a critical role in degrading the cartilage matrix (McInnes & Schett, 2011; Smolen et al., 2016).

Cells within the inflammatory infiltrate, particularly T cells, stimulate osteoclastogenesis. This process increases bone resorptive activity, resulting in juxta-articular osteopenia and the formation of bone erosions. The enhanced osteoclastogenic activity is driven by proinflammatory cytokines and the receptor activator of nuclear factor kappa-B ligand (RANKL), which are produced within the inflamed synovium (Johns Hopkins Arthritis Center, n.d.; Alpizar-Rodriguez & Lauper, 2021).

RA is initiated by an autoimmune response, where the immune system mistakenly attacks the body's own tissues. Genetic predisposition, notably the presence of HLA-DR4 alleles, plays a critical role in this aberrant immune response. Environmental factors such as smoking and microbial infections can trigger or exacerbate the disease (McInnes & Schett, 2011; Smolen et al., 2016).

Systemic Inflammation: RA is not confined to the joints; it can cause systemic inflammation affecting multiple organs. This can lead to comorbidities such as cardiovascular disease, interstitial lung disease, and osteoporosis. Systemic inflammation is driven by the same cytokines involved in synovitis, emphasizing the need for comprehensive management of RA (Gibofsky, 2014; World Health Organization, 2023).

Genetic Factors Genetic: predisposition is a significant factor in RA, with several genetic loci identified as contributors. The HLA-DRB1 gene is the most notable, associated with both susceptibility and severity of the disease. Other genes involved in immune regulation and inflammation also contribute to the pathogenesis of RA (Almutairi et al., 2021; Finckh et al., 2022).

Autoimmune Response: In a healthy immune system, white blood cells protect the body from infections and diseases. However, in RA, these cells overreact to internal stimuli and produce antibodies against the body's own tissues. This results in the destruction of healthy tissue. When the immune response affects multiple organs, the disease is termed a systemic autoimmune disease, such as lupus. When it targets a single organ or type of tissue, it is referred to as a localized autoimmune disease, such as type 1 diabetes. Autoimmune diseases often cluster in families and can affect almost any organ, causing abnormal growth or changes in function.

Citrullinated Proteins and Autoantigens: In RA, the body's immune system responds to citrullinated proteins, which are considered true auto-antigens. Citrullination is a post-translational modification of proteins, converting arginine residues into citrulline. This modification is often recognized as foreign by the immune system in RA patients. The cyclic citrullinated peptides (CCP) are used as surrogate target antigens in RA diagnosis.

Diagnostic Assays: The first-generation anti-CCP assay (anti-CCP1) was based on citrulline-containing peptides from the filaggrin sequence. Filaggrin is a protein involved in epidermal differentiation and hydration and is found only in epithelial cells, not in joints. This test had a diagnostic sensitivity of approximately 70% and a disease specificity of 96%. Despite its high specificity, filaggrin is not present in the joints, so other citrullinated proteins were thought to drive the autoimmune response in RA. To improve diagnostic accuracy, the anti-CCP2 assay was developed and is now widely used in diagnostic laboratories for its enhanced sensitivity and specificity.

RISK FACTORS AND CAUSES OF RHEUMATOID ARTHRITIS:

1. Genetic Factors:

Family History: Having a family member with RA increases the risk of developing the disease. **Genetic Markers**: Certain genetic markers, such as the HLA-DRB1 gene, are associated with a higher risk of RA.

2. Environmental Factors:

Smoking: Smoking is a significant risk factor for RA, especially in individuals with a genetic predisposition. **Infections**: Some infections may trigger RA in genetically susceptible individuals. **Air Pollution**: Exposure to air pollution has been linked to an increased risk of RA. L**ifestyle Factors- Age**: The risk of developing RA increases with age, although it can occur at any age. **Sex**: RA is more common in women than in men. **Obesity**: Being overweight or obese can increase the risk of developing RA.

3. Other Factors:

Hormonal Factors: Hormonal changes, particularly in women, may influence the development and progression of RA. **Epigenetic Changes**: Lifestyle factors such as diet and exercise can affect gene expression and potentially influence the risk of RA.

CONCLUSION:

Rheumatoid arthritis (RA) is a debilitating autoimmune disease characterized by progressive joint damage, leading to cartilage and bone destruction. The pathomechanisms of RA are complex, involving genetic predisposition, environmental factors, and immune system dysregulation. Understanding these factors is crucial for early identification and effective management of the disease.

Environmental pollutants, smoking, and hormonal changes, along with genetic markers like HLA-DRB1, play significant roles in the development and progression of RA. Chronic synovial inflammation, driven by proinflammatory cytokines and the formation of pannus, leads to joint damage. The immune system's response to citrullinated proteins, identified through anti-CCP assays, provides valuable diagnostic information.

Current biomarkers and clinical measures, such as elevated CRP levels and the number of swollen and tender joints, are essential for early detection. The development of more sensitive biochemical markers can further enhance the management of RA by facilitating the appropriate use of targeted therapies, thus reducing the progression of joint damage.

Future research should continue to focus on understanding the exact mechanisms and risk factors of RA, aiming to prevent disease onset and progression. By identifying and mitigating these risk factors, we can improve the quality of life for individuals with RA and prevent irreversible damage to the joints and other affected organs.

CONFLICT OF INTEREST: No

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