

Inflammatory Cytokines and Bone Health in Ankylosing Spondylitis

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Abstract

Ankylosing Spondylitis (AS) is a chronic inflammatory autoimmune disorder primarily affecting the axial skeleton, sacroiliac joints, and spinal structures. The disease is characterized by persistent inflammation, progressive pain, stiffness, reduced spinal mobility, and abnormal bone remodeling that may eventually result in spinal fusion and severe disability. Inflammatory cytokines play a critical role in the development and progression of AS by regulating immune responses, osteoclast activation, and pathological new bone formation. The interaction between chronic inflammation and bone metabolism contributes significantly to skeletal complications such as osteoporosis, syndesmophyte formation, and structural joint damage in AS patients. The present review aims to evaluate the role of major inflammatory cytokines in bone health and disease progression in Ankylosing Spondylitis. Particular emphasis has been placed on cytokines such as tumor necrosis factor- α (TNF- α), interleukin-17 (IL-17), interleukin-6 (IL-6), and the IL-23/IL-17 signaling axis. The review also discusses the involvement of the RANK/RANKL/OPG pathway and oxidative stress in inflammatory bone damage and skeletal remodeling. Current evidence indicates that inflammatory cytokines significantly influence both bone destruction and abnormal new bone formation in AS. Cytokine dysregulation alters osteoblast and osteoclast activity, resulting in impaired skeletal homeostasis and progressive structural damage. Cytokine-targeted therapies such as TNF inhibitors and IL-17 inhibitors have demonstrated considerable effectiveness in reducing inflammation and slowing disease progression.

Keywords : Ankylosing Spondylitis, Cytokines, Bone Health, TNF- α , IL-17, IL-6, Osteoporosis, Inflammation

Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory rheumatic disorder belonging to the group of spondyloarthropathies. It mainly affects the axial skeleton, including the spine and sacroiliac joints, causing chronic pain, stiffness, reduced mobility, and progressive skeletal deformity. The disease commonly develops in young adults and significantly affects physical function and quality of life. Persistent inflammation in spinal structures eventually leads to pathological new bone formation and fusion of vertebrae, resulting in severe disability in advanced stages of the disease. AS is strongly associated with genetic susceptibility, particularly the HLA-B27 gene, although environmental and immunological factors also contribute to disease development. The disease affects males more frequently than females and is generally diagnosed between the ages of 20 and 40 years. In addition to skeletal involvement, AS may also present with extra-articular manifestations such as uveitis, inflammatory bowel disease, psoriasis, and cardiovascular complications. Delayed diagnosis remains a major challenge because early symptoms are often nonspecific and mistaken for mechanical back pain. The pathogenesis of AS involves complex interactions between genetic predisposition, immune dysregulation, chronic inflammation, and abnormal bone remodeling. Immune cells such as T lymphocytes, macrophages, and dendritic cells produce inflammatory cytokines that activate inflammatory pathways and promote tissue damage. Cytokines are small signaling proteins that regulate immune responses and play essential roles in inflammation and bone metabolism. Increased

levels of inflammatory cytokines such as TNF- α , IL-17, IL-6, and IL-23 are strongly associated with disease activity and structural progression in AS patients.

One of the most distinctive features of AS is the coexistence of bone destruction and pathological new bone formation. Chronic inflammation stimulates osteoclast-mediated bone resorption, increasing the risk of osteoporosis and vertebral fractures. Simultaneously, inflammatory pathways activate osteoblasts, resulting in excessive bone formation and syndesmophyte development. Progressive ossification of spinal ligaments and joints eventually leads to spinal fusion and reduced flexibility. This imbalance between bone formation and bone resorption makes AS a unique inflammatory bone disease.

Inflammatory cytokines play central roles in regulating these pathological skeletal changes. TNF- α is one of the most important cytokines involved in AS pathogenesis and contributes to inflammatory cell recruitment, cytokine production, osteoclast activation, and bone erosion. IL-17 promotes both inflammation and pathological bone formation, while IL-6 influences osteoclast differentiation and systemic inflammatory responses. The IL-23/IL-17 axis has emerged as a major immunological pathway involved in disease progression and structural damage in AS. The RANK/RANKL/OPG signaling pathway is another critical regulator of bone metabolism in Ankylosing Spondylitis. Receptor activator of nuclear factor-kappa B ligand (RANKL) stimulates osteoclast formation and bone resorption, while osteoprotegerin (OPG) acts as a protective decoy receptor that inhibits osteoclast activation. Cytokine-induced imbalance in this pathway contributes to bone loss and skeletal abnormalities observed in AS patients.

Oxidative stress also plays an important role in disease progression and bone metabolism. Increased production of reactive oxygen species contributes to inflammatory tissue damage and enhances osteoclast activity, leading to bone loss and structural complications. The interaction between oxidative stress and inflammatory cytokines further amplifies disease severity and skeletal deterioration. Recent advances in immunology and molecular biology have improved understanding of cytokine-mediated mechanisms in AS and have contributed to the development of targeted biologic therapies. TNF inhibitors and IL-17 inhibitors have shown significant effectiveness in reducing inflammation, improving mobility, and slowing radiographic progression. These therapeutic developments highlight the importance of cytokine research in improving clinical outcomes and personalized treatment strategies for AS patients. The present review was undertaken to critically analyze the relationship between inflammatory cytokines and bone health in Ankylosing Spondylitis. The review focuses on the roles of TNF- α , IL-17, IL-6, the IL-23/IL-17 axis, oxidative stress, and bone remodeling pathways in disease progression and skeletal complications. It also examines the clinical significance of cytokine-targeted therapies and identifies current research gaps and future directions in the management of AS.

Review of Literature

Ankylosing Spondylitis is a chronic immune-mediated inflammatory disorder characterized by inflammation of the axial skeleton, progressive structural damage, and abnormal bone remodeling. Recent advances in immunology have demonstrated that inflammatory cytokines play a central role in disease development and progression. Cytokines regulate immune cell activation, inflammatory signaling pathways, osteoclast differentiation, and osteoblast activity, thereby influencing both inflammation and skeletal changes in AS patients. The immunopathology of Ankylosing Spondylitis involves complex interactions between innate and adaptive immune systems. Activated macrophages, dendritic cells, neutrophils, and T lymphocytes produce pro-inflammatory cytokines that contribute to chronic inflammation and tissue destruction. Genetic susceptibility, especially the presence of the HLA-B27 gene, strongly influences immune dysregulation in AS. Misfolding of HLA-B27 molecules may trigger abnormal immune responses and activation of inflammatory cytokine pathways. Increased

infiltration of immune cells into spinal joints and entheses leads to persistent inflammation and progressive skeletal damage.

Inflammatory cytokine networks are essential in the pathogenesis of autoimmune and inflammatory disorders. Cytokines such as TNF- α , IL-17, IL-6, IL-23, and interferon-gamma regulate communication between immune cells and influence inflammatory responses. In AS, these cytokines create a pro-inflammatory environment that promotes tissue injury, osteoclast activation, and pathological bone formation. Dysregulated cytokine signaling contributes to disease activity, pain, stiffness, and structural progression. Tumor necrosis factor-alpha (TNF- α) is one of the most extensively studied cytokines in Ankylosing Spondylitis. TNF- α is produced by activated macrophages and T cells and plays a major role in inflammatory responses. Elevated levels of TNF- α are commonly observed in AS patients and correlate with disease severity and radiographic progression. TNF- α stimulates inflammatory cell recruitment, cytokine production, and activation of osteoclasts, leading to bone erosion and tissue damage. Chronic TNF- α -mediated inflammation also contributes to systemic complications such as osteoporosis and increased fracture risk.

The introduction of TNF inhibitors has revolutionized the treatment of Ankylosing Spondylitis. Drugs such as infliximab, etanercept, adalimumab, and golimumab significantly reduce inflammation, pain, and disease activity. These biologic therapies improve physical function and quality of life while slowing structural progression in many patients. However, some individuals show inadequate response to TNF inhibitors, indicating involvement of additional inflammatory pathways in disease pathogenesis. Interleukin-17 (IL-17) has emerged as another critical cytokine involved in AS progression. IL-17 is mainly produced by Th17 cells and contributes to inflammatory responses, neutrophil recruitment, and cytokine amplification. Increased IL-17 expression has been observed in spinal tissues, peripheral blood, and synovial fluid of AS patients. IL-17 promotes both inflammation and pathological new bone formation, making it particularly important in AS compared to other inflammatory arthritic disorders.

IL-17 stimulates osteoblast activity and contributes to syndesmophyte formation and spinal ankylosis. At the same time, it enhances inflammatory responses and tissue damage by inducing production of other cytokines and chemokines. IL-17 inhibitors such as secukinumab and ixekizumab have demonstrated significant clinical benefits in reducing inflammation and improving mobility in AS patients. These findings highlight the importance of IL-17 as both a biomarker and therapeutic target in Ankylosing Spondylitis. Interleukin-6 (IL-6) is another important inflammatory cytokine associated with bone metabolism and immune activation. IL-6 promotes differentiation of osteoclasts through activation of the RANK/RANKL signaling pathway, leading to increased bone resorption and osteoporosis. Elevated IL-6 levels are associated with systemic inflammation, fatigue, and disease activity in AS patients. Chronic IL-6-mediated inflammation contributes to skeletal complications and reduced bone mineral density.

The IL-23/IL-17 axis is currently recognized as one of the most important immunological pathways involved in AS pathogenesis. IL-23 promotes differentiation and survival of Th17 cells, which subsequently produce IL-17 and other pro-inflammatory cytokines. Activation of the IL-23/IL-17 pathway contributes to chronic inflammation, enthesitis, and abnormal bone remodeling. Genetic and experimental studies strongly support the involvement of this pathway in disease progression and structural damage in AS.

The RANK/RANKL/OPG pathway plays a major role in regulating bone metabolism in inflammatory disorders. RANKL stimulates osteoclast differentiation and activation, resulting in bone resorption and skeletal damage. Osteoprotegerin acts as a protective inhibitor that blocks RANKL-mediated osteoclast activation. In AS, inflammatory cytokines increase RANKL expression and disrupt the balance between

bone formation and bone resorption. This imbalance contributes to osteoporosis, vertebral fractures, and structural deformities observed in AS patients. Oxidative stress is another important factor contributing to inflammatory tissue damage and abnormal bone metabolism in Ankylosing Spondylitis. Increased production of reactive oxygen species enhances inflammatory cytokine activity and promotes osteoclast differentiation. Oxidative stress also damages cellular structures and accelerates tissue injury in spinal joints and entheses. Studies have demonstrated elevated oxidative stress markers in AS patients, suggesting their involvement in disease severity and skeletal complications.

Methodology

The present study was conducted as a narrative review to evaluate the relationship between inflammatory cytokines and bone health in Ankylosing Spondylitis (AS). The review aimed to analyze existing scientific literature concerning the role of inflammatory cytokines in disease pathogenesis, bone remodeling, osteoporosis, structural damage, and therapeutic interventions in AS patients. A narrative review design was selected because it allows comprehensive discussion and critical of findings from multiple experimental, clinical, and review studies related to cytokine-mediated skeletal changes in Ankylosing Spondylitis. Relevant literature for the review was collected from internationally recognized scientific databases including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. These databases were selected because they provide extensive access to peer-reviewed biomedical, rheumatological, immunological, and molecular research publications. Articles published between 2010 and 2026 were primarily considered to ensure inclusion of recent developments and updated scientific evidence regarding inflammatory cytokines and bone metabolism in AS.

The inclusion criteria involved peer-reviewed original research articles, clinical studies, review papers, meta-analyses, and experimental investigations related to inflammatory cytokines and skeletal changes in Ankylosing Spondylitis. Studies discussing the roles of TNF- α , IL-17, IL-6, IL-23, RANK/RANKL/OPG pathways, oxidative stress, osteoporosis, and biologic therapies in AS were included. Both human and animal studies were considered if they provided relevant insights into cytokine-mediated inflammatory mechanisms and bone remodeling processes. The exclusion criteria included duplicate publications, conference abstracts without full text, studies unrelated to cytokine involvement in AS, articles lacking adequate methodological details, and publications written in languages other than English. Studies focused solely on non-inflammatory mechanisms or unrelated rheumatological disorders were also excluded from the review process. A systematic search strategy was adopted using relevant keywords and combinations of medical subject terms associated with the topic. The major keywords used during literature search included “Ankylosing Spondylitis,” “Inflammatory Cytokines,” “TNF- α ,” “IL-17,” “IL-6,” “Bone Health,” “Osteoporosis,” “Bone Remodeling,” “RANKL,” “Inflammation,” “Osteoclasts,” “Syndesmophytes,” and “Autoimmune Disease.” Boolean operators such as AND, OR, and NOT were applied to refine the search results and improve relevance of the selected studies.

4. Inflammatory Cytokines and Bone Health in AS

Table 4.1 Major Inflammatory Cytokines in Ankylosing Spondylitis

Cytokine	Primary Source	Major Functions in AS	Effect on Bone Health
TNF- α	Macrophages, T cells	Promotes inflammation and immune activation	Causes bone erosion and osteoporosis

IL-17	Th17 cells	Enhances inflammatory responses	Promotes both bone loss and new bone formation
IL-6	Macrophages, fibroblasts	Stimulates acute inflammatory response	Increases osteoclast activity
IL-23	Dendritic cells	Maintains Th17 cell survival	Contributes to enthesitis and bone remodeling
IL-1 β	Activated macrophages	Enhances inflammatory signaling	Stimulates cartilage and bone destruction

The table demonstrates that multiple inflammatory cytokines contribute significantly to the pathogenesis of Ankylosing Spondylitis. TNF- α , IL-17, IL-6, and IL-23 are central mediators of chronic inflammation and abnormal skeletal remodeling. These cytokines influence both osteoclast and osteoblast activity, resulting in simultaneous bone erosion and pathological new bone formation. Their elevated expression levels are strongly associated with disease severity and structural progression in AS patients.

Table 4.2 Role of TNF- α in Bone Destruction in AS

Mechanism	Biological Effect	Clinical Outcome
Activation of osteoclasts	Increased bone resorption	Osteoporosis and vertebral fractures
Cytokine amplification	Chronic inflammation	Persistent spinal pain and stiffness
Synovial inflammation	Tissue destruction	Structural joint damage
RANKL stimulation	Enhanced osteoclast differentiation	Bone erosion
Immune cell recruitment	Increased inflammatory infiltration	Disease progression

TNF- α is one of the most important cytokines involved in inflammatory and skeletal damage in Ankylosing Spondylitis. It promotes osteoclast-mediated bone resorption and stimulates inflammatory pathways responsible for chronic pain and tissue destruction. Increased TNF- α activity contributes significantly to osteoporosis, vertebral fractures, and progressive spinal damage. These findings explain the clinical effectiveness of TNF inhibitors in reducing disease activity and improving skeletal outcomes.

Table 4.3 Role of IL-17 in Pathological Bone Formation

IL-17 Activity	Pathological Effect	Clinical Significance
Activation of inflammatory pathways	Increased cytokine production	Persistent inflammation
Osteoblast stimulation	New bone formation	Syndesmophyte development
Osteoclast activation	Bone resorption	Reduced bone mineral density

Enthesitis promotion	Ligament inflammation	Reduced spinal mobility
Interaction with IL-23	Amplified immune response	Disease progression

IL-17 plays a unique role in Ankylosing Spondylitis by contributing to both inflammatory bone destruction and pathological new bone formation. Increased IL-17 activity promotes syndesmophyte development and spinal ankylosis while simultaneously increasing inflammatory damage and osteoporosis risk. The dual role of IL-17 highlights its importance as a therapeutic target in modern biologic treatment strategies.

Table 4.4 IL-6 and Osteoclast Activation in AS

Mechanism of IL-6 Action	Effect on Bone Metabolism	Clinical Outcome
RANKL pathway activation	Increased osteoclast differentiation	Bone loss
Cytokine amplification	Systemic inflammation	Disease flare-ups
Acute-phase response stimulation	Elevated inflammatory markers	Increased disease activity
Osteoclast maturation	Enhanced bone resorption	Osteoporosis
Immune activation	Chronic inflammation	Skeletal complications

IL-6 significantly contributes to inflammatory bone loss in Ankylosing Spondylitis through activation of osteoclasts and enhancement of inflammatory pathways. Elevated IL-6 levels are commonly associated with systemic inflammation, disease severity, and reduced bone mineral density. Chronic IL-6-mediated inflammation therefore increases the risk of osteoporosis and skeletal fragility in AS patients.

Table 4.5 IL-23/IL-17 Axis in AS Pathogenesis

Pathway Component	Functional Role	Impact on Disease Progression
IL-23	Maintains Th17 cell survival	Sustains chronic inflammation
Th17 Cells	Produce IL-17 cytokines	Amplify immune responses
IL-17	Promotes inflammatory signaling	Causes tissue damage
Enthesitis	Inflammation at tendon insertion sites	Structural skeletal changes
Cytokine Cascade	Activates additional inflammatory mediators	Progressive spinal ankylosis

The IL-23/IL-17 signaling axis is a major immunological pathway involved in Ankylosing Spondylitis. Persistent activation of this pathway contributes to enthesitis, chronic inflammation, and pathological bone remodeling. Genetic and clinical studies strongly support the role of the IL-23/IL-17 axis in disease progression, making it an important target for biologic therapies.

Table 4.6 RANK/RANKL/OPG Pathway and Bone Remodeling

Component	Function	Effect in AS
RANK	Receptor on osteoclast precursor cells	Promotes osteoclast activation
RANKL	Stimulates osteoclast differentiation	Increases bone resorption
OPG	Inhibits RANKL activity	Protects against bone loss
Cytokine-Induced RANKL	Enhanced inflammatory signaling	Excessive bone destruction
Reduced OPG Activity	Loss of protective effect	Osteoporosis and fractures

The RANK/RANKL/OPG pathway is a critical regulator of bone metabolism in Ankylosing Spondylitis. Inflammatory cytokines increase RANKL expression and reduce the protective effects of OPG, leading to excessive osteoclast activation and bone resorption. This imbalance contributes to osteoporosis, vertebral fractures, and structural skeletal damage commonly observed in AS patients.

Table 4.7 Oxidative Stress and Bone Metabolism in AS

Oxidative Stress Factor	Biological Effect	Clinical Impact
Reactive oxygen species	Cellular damage	Tissue inflammation
Lipid peroxidation	Membrane injury	Joint destruction
Oxidative cytokine activation	Enhanced inflammation	Increased disease severity
Osteoclast stimulation	Increased bone resorption	Reduced bone density
Reduced antioxidant defense	Chronic oxidative damage	Structural progression

Oxidative stress contributes significantly to inflammatory tissue damage and abnormal bone metabolism in Ankylosing Spondylitis. Increased production of reactive oxygen species enhances inflammatory cytokine activity and osteoclast differentiation, resulting in progressive bone loss and skeletal complications. Reduced antioxidant defense mechanisms further worsen disease severity and structural damage.

Table 4.8 Cytokine-Targeted Therapies in Ankylosing Spondylitis

Therapeutic Agent	Target Cytokine	Major Clinical Benefits
Infliximab	TNF- α	Reduces inflammation and pain
Adalimumab	TNF- α	Improves spinal mobility
Etanercept	TNF- α	Decreases disease activity
Secukinumab	IL-17	Prevents pathological bone formation
Ixekizumab	IL-17	Improves physical function

Cytokine-targeted biologic therapies have significantly improved management of Ankylosing Spondylitis. TNF inhibitors effectively suppress inflammation and reduce disease activity, while IL-17 inhibitors help control both inflammatory damage and pathological new bone formation. These therapies represent major advancements in personalized treatment strategies for AS patients.

Table 4.9 Relationship Between Cytokines and Bone Complications in AS

Cytokine	Bone Complication	Associated Clinical Outcome
TNF- α	Osteoporosis	Increased fracture risk
IL-17	Syndesmophyte formation	Spinal ankylosis
IL-6	Reduced bone mineral density	Skeletal fragility
IL-23	Enthesitis	Structural progression
RANKL	Bone erosion	Joint deformity

Different inflammatory cytokines contribute to distinct skeletal complications in Ankylosing Spondylitis. TNF- α and IL-6 are mainly associated with osteoporosis and bone loss, while IL-17 contributes significantly to syndesmophyte formation and spinal fusion. Understanding cytokine-specific skeletal effects is essential for selecting appropriate targeted therapies and preventing irreversible structural damage. The findings presented in the tables clearly indicate that inflammatory cytokines are major regulators of bone metabolism and structural progression in Ankylosing Spondylitis. Cytokines such as TNF- α , IL-17, IL-6, and IL-23 contribute significantly to chronic inflammation, osteoclast activation, osteoporosis, syndesmophyte formation, and spinal ankylosis. The interaction between inflammatory signaling pathways and bone remodeling mechanisms leads to the coexistence of bone loss and pathological new bone formation, which is a hallmark feature of AS.

Discussion

Ankylosing Spondylitis (AS) is a chronic inflammatory autoimmune disorder characterized by persistent inflammation, progressive spinal stiffness, abnormal bone remodeling, and skeletal complications. The present review highlights the significant role of inflammatory cytokines in the pathogenesis of AS and their influence on bone metabolism and structural progression. Cytokines such as TNF- α , IL-17, IL-6, and IL-23 have emerged as major mediators of inflammation, osteoclast activation, osteoporosis, and pathological new bone formation in AS patients. One of the most important findings of this review is the dual role of inflammatory cytokines in causing both bone destruction and pathological new bone formation. Unlike many other inflammatory arthritic disorders, AS is characterized by coexistence of osteoporosis and excessive bone growth. TNF- α and IL-6 contribute significantly to osteoclast-mediated bone resorption, resulting in reduced bone mineral density and increased fracture risk. Simultaneously, IL-17 and the IL-23/IL-17 axis stimulate osteoblast activity and syndesmophyte formation, eventually leading to spinal ankylosis and structural deformity. TNF- α plays a central role in inflammatory tissue damage and skeletal complications in AS. Elevated TNF- α levels are strongly associated with disease activity, chronic pain, and radiographic progression. TNF- α promotes inflammatory cell recruitment and activation of osteoclasts through the RANK/RANKL pathway. Persistent TNF-mediated inflammation therefore contributes to both systemic osteoporosis and localized bone erosion. The clinical effectiveness of TNF inhibitors strongly supports the importance of TNF- α in disease progression and skeletal deterioration. IL-17 has emerged as another critical cytokine involved in both inflammation and pathological new bone formation.

Increased IL-17 expression promotes chronic inflammatory responses, enthesitis, and activation of bone remodeling pathways. IL-17 also contributes to syndesmophyte development and spinal fusion, which are hallmark features of advanced AS. The development of IL-17 inhibitors such as secukinumab and ixekizumab has significantly improved treatment outcomes in patients with inadequate response to TNF inhibitors.

IL-6 contributes mainly to osteoclast activation and inflammatory amplification. Elevated IL-6 levels are associated with disease severity, fatigue, and systemic inflammation. Chronic IL-6-mediated activation of the RANK/RANKL signaling pathway enhances bone resorption and contributes to osteoporosis and skeletal fragility in AS patients. These findings demonstrate that inflammatory cytokines not only regulate immune responses but also directly influence bone metabolism and structural integrity. The review also emphasizes the importance of the IL-23/IL-17 signaling axis in AS pathogenesis. Activation of this pathway promotes differentiation and survival of Th17 cells, resulting in increased production of IL-17 and other inflammatory mediators. Persistent activation of the IL-23/IL-17 axis contributes to enthesitis, chronic inflammation, and pathological bone remodeling. Genetic studies identifying IL-23 receptor polymorphisms further support the involvement of this pathway in disease susceptibility and progression.

Major Findings

The present review identified inflammatory cytokines as major contributors to the pathogenesis and skeletal complications of Ankylosing Spondylitis. Cytokines such as TNF- α , IL-17, IL-6, and IL-23 were found to play central roles in chronic inflammation, osteoclast activation, pathological bone formation, and structural progression in AS patients. TNF- α emerged as one of the most significant cytokines associated with inflammatory tissue damage, bone erosion, osteoporosis, and disease severity. Elevated TNF- α levels contribute to osteoclast-mediated bone resorption through activation of the RANK/RANKL signaling pathway. IL-17 was identified as another critical cytokine involved in both inflammatory damage and pathological new bone formation. Increased IL-17 expression contributes to syndesmophyte formation, spinal ankylosis, and chronic inflammation in AS patients. The review further demonstrated that IL-6 significantly contributes to osteoclast activation and reduced bone mineral density, thereby increasing the risk of osteoporosis and vertebral fractures. The IL-23/IL-17 axis was recognized as a major immunological pathway responsible for maintaining chronic inflammation and abnormal skeletal remodeling in Ankylosing Spondylitis.

Conclusion

Ankylosing Spondylitis is a chronic inflammatory autoimmune disorder characterized by persistent inflammation, abnormal bone remodeling, and progressive structural damage. The present review demonstrates that inflammatory cytokines play central roles in disease pathogenesis, skeletal complications, and progression of Ankylosing Spondylitis. Cytokines such as TNF- α , IL-17, IL-6, and IL-23 significantly influence immune activation, osteoclast differentiation, osteoblast activity, and bone metabolism. The review highlights the complex relationship between inflammation and bone health in AS. Chronic cytokine-mediated inflammation contributes to osteoporosis, bone erosion, syndesmophyte formation, and spinal ankylosis. The coexistence of bone loss and pathological new bone formation represents one of the most distinctive pathological features of the disease. Important molecular pathways such as the IL-23/IL-17 axis and the RANK/RANKL/OPG signaling pathway further regulate skeletal remodeling and structural progression in AS patients. Recent advances in cytokine research have significantly improved understanding of disease mechanisms and therapeutic approaches. Cytokine-targeted biologic therapies, particularly TNF inhibitors and IL-17 inhibitors, have transformed the management of Ankylosing Spondylitis by reducing inflammation, improving

physical function, preserving bone health, and slowing radiographic progression. These therapies highlight the importance of inflammatory cytokines as both biomarkers and therapeutic targets.

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