MEDDOCS
Open Access Publisher

ISSN: 2637-4900

Journal of Community Medicine

Open Access | Review Article

Ankylosing Spondylitis: Recent Advances and Insights

Gaurav Verma[1]; Shaminder Kaur[2]; Priyanka Kashyap[3]; Pankaj Kumar[2]; Gaganjit Kaur[1]; Bhumika Sharma[1]; Amanpreet Kaur[1]; Qaisar Farooq[1]; Harpreet Singh[1]*

[1]School of Health Sciences, CT University, Ludhiana, Punjab, India.

[2]School of Allied Health Sciences, CT University, Ludhiana, Punjab, India.

[3]Department of Microbiology, Ras Bihari Bose Subharti University, Dehradun, Uttrakhand, India.

***Corresponding Author(s): Gaurav Verma**
School of Health Sciences, CT University, Ludhiana, Punjab, India.
Email: gaurav.verma9557@gmail.com

Received: July 22, 2025
Accepted: Sep 19, 2025
Published Online: Sep 26, 2025
Journal: Journal of Community Medicine
Publisher: MedDocs Publishers LLC
Online edition: http://meddocsonline.org/
Copyright: © Verma G (2025). *This Article is distributed under the terms of Creative Commons Attribution 4.0 International License*

Keywords: Ankylosing spondylitis; IL-17; AS; TNF; MRI; HLA-B27; Inflammation; Sacroiliac joints; Pain; Stiffness.

Abstract

AS (Ankylosing spondylitis) is a chronic inflammatory disease primarily affecting the spine and sacroiliac joints, leading to pain and stiffness. Recent advances in our understanding of AS have illuminated its pathophysiology, highlighting the role of genetic factors, particularly the HLA-B27 allele, and the immune system's contribution to inflammation. Innovations in imaging techniques, such as MRI, have enhanced early diagnosis, while the development of biologic therapies targeting Tumor Necrosis Factor (TNF) and interleukin pathways has revolutionized treatment options, significantly improving patient outcomes. Furthermore, ongoing research into novel therapeutic strategies and biomarkers promises to refine management approaches. This review consolidates current insights into the mechanisms, clinical manifestations and treatment paradigms of AS, emphasizing the importance of personalized care and early intervention to optimize long-term results for affected individuals.

Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory illness that chiefly targets the spine and pelvis, leading to discomfort and a significant loss of mobility. Traditionally, the understanding of AS was limited, when often resulted in late diagnoses and inadequate treatment measures [1]. Initial therapeutic interventions largely consisted of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and physical therapy, aimed at symptom relief and functional maintenance [2].

A significant advancement in the understanding of AS was achieved with the discovery of the HLA-B27 antigen, which confirmed a genetic association with the disease [2]. This important breakthrough has opened new research pathways into the immunological mechanisms involved, shedding light on the various inflammatory pathways that contribute to disease progression and the roles of both innate and adaptive immune responses [3].

In recent years, there have been significant improvements in patient outcomes due to advancements in treatment. The emergence of biologic therapies, notably Tumor Necrosis Factor (TNF) inhibitors, has revolutionized the approach to managing AS delivering effective symptom relief and mitigating structural damage. Furthermore, innovative treatments that target Interleukin-17 (IL-17) and other inflammatory mediators have been developed, providing additional options for patients unresponsive to standard therapies [3,4].

This review article aims to advance our knowledge of AS by investigating the complex relationships between genetic, environmental, and psychosocial factors. Understanding these dynamics is vital for creating tailored treatment options that meet the distinct needs of those living with AS [4,5]. The review will discuss the historical context, recent innovations, and current research directions in Ankylosing spondylitis, showcasing the progress made and the future opportunities in this rapidly evolving field [5,6].

Cite this article: Gaurav V, Shaminder K, Priyanka K, Pankaj K, Gaganjit K, et al. Ankylosing Spondylitis: Recent Advances and Insights. J Community Med. 2025; 8(2): 1055.

Genetics of ankylosing spondylitis

Historical perspective

In the mid-20th century, the understanding of AS began to progress significantly with the identification of the HLA-B27 antigen, which highlighted a genetic link to the disease. This pivotal discovery shifted research priorities towards exploring immunological mechanisms, enhancing knowledge of the inflammatory processes that underpin AS. Early therapeutic strategies predominantly relied on Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), which offered symptomatic relief but did not address the fundamental inflammation or prevent the advancement of the disease [4-6].

AS is characterized by its intricate and multifactorial nature, with a notable genetic aspect. Delving into the genetic factors associated with AS has been essential for understanding its pathogenesis and enhancing diagnostic and treatment methodologies [7].

HLA-B27 and genetic predisposition

The strongest genetic association with AS is the presence of HLA-B27 antigen. Approximately 90% of individuals with AS test positive for this antigen, compared to about 5-10% of the general population. The presence of HLA-B27 is considered a significant individuals will develop the disease, indicating that other genetic and environmental factors play a role [7,8].

Other genetic factors

HLA-B27 is recognized as the most prominent genetic marker for AS, but recent studies have uncovered other loci that are also associated with the condition. Genome-Wide Association Studies (GWAS) have identified a variety of Single Nucleotide Plymorphisms (SNPs) that correlate with the disease [7-9]. Significant genetic regions include:

1. **ERAP1:** This gene is responsible for encoding an enzyme that plays a crucial role in the processing of antigens for T cell presentation. Variants within the ERAP1 gene are believed to affect immune responses and have been linked to susceptibility to AS [10].
2. **IL-23R:** Genetic variations in the interleukin-23 receptor gene have been associated with AS, underscoring the significance of the IL-23/IL-17 signaling pathway in the inflammatory mechanisms of the disease [10].
3. **Other loci:** Numerous additional genes associated with immune function, including IL-1, IL-6, and TNF, have been identified as contributing factors to the susceptibility of AS through findings from genome-wide association studies (GWAS) [11].

Genome-wide association studies indicate that the T helper 17/23 (Th17/23) axis, along with its various genetic polymorphisms, plays a role not only in AS but also in Inflammatory Bowel Disease (IBD) and psoriasis. This supports the notion of a shared pathogenic mechanism, with evidence suggesting that the microbiome may be involved in the progression of these conditions [12].

Pathophysiology of ankylosing spondylitis

Recent studies has shed light on the complex pathophysiology of AS, which is marked by an atypical immune response, especially within the innate immune system. [13] This autoimmune condition predominantly impacts the sacroiliac joints and the spine, although it may also affect other peripheral joints and entheses, the areas where tendons or ligaments attach to the bone. In addition, progress in imaging technologies, especially magnetic resonance imaging (MRI), has enhanced the early identification of sacroiliitis and other inflammatory changes, facilitating timely intervention [14,15].

Immune system dysregulation: AS is linked to genetic factors particularly the HLA-B27 gene which is essential in triggering the immune system's activity. While having this gene alone does not guarantee the onset of the disease, it notably heightens the likelihood of developing AS. Recent studies indicate that individuals carrying the HLA-B27 gene are more prone to unusual interactions between their immune system and gut Microbiome resulting in T-cell activation and an atypical inflammatory response [47].

Key cytokines in the inflammatory cascade: In the pathophysiology of AS, inflammatory cytokines are essential, particularly Tumor Necrosis Factor-Alpha (TNF-α) and Interleukin-17 (IL-17). These cytokines are crucial in driving inflammation in the joints and entheses.

- TNF-α serves as a key mediator of inflammation in Ankylosing Spondylitis (AS). It initiates the release of additional pro-inflammatory cytokines and plays a significant role in both bone destruction and the formation of new bone through the activation of osteoclasts.
- IL-17 which is mainly produced by Th17 cells, enhances the inflammatory response, leading to tissue damage and irregular bone formation. The involvement of IL-17 is especially prominent in the development of syndesmophytes, the bony outgrowths associated with AS that can result in spinal fusion [48].

1. Bone remodeling: erosion and new bone formation

One of the key features of AS is the phenomenon of bony remodeling characterized by both bone erosion and the formation of new bone. This process is triggered by the activation of the innate immune system, which allows immune cells such as macrophages and neutrophils to infiltrate the affected joints. These cells produce pro-inflammatory cytokines including TNF and IL-17 that activate osteoclasts, resulting in bone resorption. At the same time osteoblasts are stimulated to create new bone at the enthesis, which can eventually lead to the formation of syndesmophytes, causing spinal fusion and a significant reduction in mobility in severe instances [14,49].

Microbiome and ankylosing spondylitis

Recent studies have started to clarify the connection between the gut microbiome and AS, indicating that changes in gut microbiota could affect the initiation and advancement of the disease. The gut microbiome is essential for regulating the immune system, and dysbiosis, which refers to an imbalance in microbial populations, has been associated with several autoimmune disorders, including AS [16].

1. Dysbiosis and immune response: Research indicates that individuals with AS frequently display dysbiosis, which is marked by a decrease in beneficial microbial populations and an increase in pro-inflammatory bacteria. This imbalance may result in heightened intestinal permeability, facilitating the entry of microbial antigens into the bloodstream and instigating systemic inflammation [16]. The gut microbiome is essential for

sustaining immune balance, and any disturbances in this intricate system can result in improper immune responses, which may lead to chronic inflammation and the advancement of various diseases. Dysbiosis is believed to play a significant role in influencing immune responses in AS through various mechanisms. A primary pathway involves the activation of Th17 cells, which are responsible for producing interleukin-17 (IL-17), a key pro-inflammatory cytokine that is crucial to the development of AS. Specific microbial species, especially those belonging to the Enterobacteriaceae family, such as Klebsiella pneumoniae, have been identified as promoters of Th17 differentiation by enhancing the production of IL-23. This, in turn, leads to further activation of Th17 cells. These activated Th17 cells contribute to the release of additional pro-inflammatory cytokines, including Tumor Necrosis Factor (TNF), which intensifies the inflammatory response in peripheral joints and entheses, resulting in the hallmark symptoms of AS, including pain, stiffness, and joint damage. [43,44].

2. Inflammatory cytokines: Certain gut microbiota are associated with the production of inflammatory cytokines, including Tumor Necrosis Factor (TNF) and interleukin-17 (IL-17), which are crucial in the pathophysiology of AS. The presence of particular bacterial species can either promote or suppress the production of these cytokines, thereby affecting the activity of the disease [17]. The interaction between HLA-B27 and the microbiome initiates systemic inflammation that transcends the gastrointestinal system, impacting various organs, including the joints. In this process, inflammatory cytokines such as IL-17 and TNF are produced by immune cells activated by microbial stimuli, significantly contributing to the inflammation observed in AS. This inflammatory response is exacerbated by dysbiosis, where an imbalance in gut microbiota compromises the intestinal barrier, permitting microbial components like Lipopolysaccharides (LPS) to enter the bloodstream and trigger systemic inflammation. This condition, often referred to as "leaky gut," has been associated with heightened inflammatory levels in AS patients [45]. Gaining insights into the interplay between HLA-B27 and the microbiome in influencing systemic inflammation may pave the way for innovative therapeutic approaches aimed at correcting microbial imbalances and modulating immune responses in AS [43].

3. HLA-B27 and the microbiome: The HLA-B27 antigen is recognized as a significant genetic risk factor for AS. Recent investigations suggest that the microbiome may interact with HLA-B27 to influence immune responses, potentially activating inflammatory pathways that contribute to the progression of the disease [18]. The relationship between HLA-B27 and the gut microbiome represents a significant focus of research aimed at elucidating the pathogenesis of AS. HLA-B27 is recognized as a primary genetic risk factor for AS, with more than 90% of diagnosed patients possessing this allele. Recent investigations indicate that HLA-B27 may affect both the composition and functionality of the gut microbiota, potentially contributing to the onset of systemic inflammation. Individuals with the HLA-B27 allele show notable changes in their gut microbiome, including an increase in specific bacterial groups such as Enterobacteriaceae, which encompasses *Klebsiella pneumoniae*. These bacteria are believed to stimulate immune activation by facilitating Th17 differentiation, a crucial pathway in the pathology of AS. This dysbiosis may foster a microbiome environment that sustains immune responses, especially in those genetically susceptible to AS. [46].

4. Therapeutic implications: Gaining insights into the microbiome's role in AS paves the way for innovative therapeutic approaches. Utilizing probiotics and dietary modifications aimed at reestablishing a balanced gut microbiota may serve as complementary strategies to traditional treatments, potentially alleviating inflammation and enhancing patient outcomes [19].

Additionally, studies on animals have indicated that HLA-B27 alone is not sufficient for the onset of AS, as transgenic rats raised in a germ-free environment did not show signs of spondyloarthritis (SpA) [20]. In the past few years, researchers have shifted their focus to identifying pathogens that may trigger AS. The first bacterium reported in this regard was *Klebsiella pneumoniae* [21] which is thought to carry an antigen resembling one produced by the HLA-B27 gene. However, the underlying mechanism is not yet fully understood, and some studies argue that its role in AS is unlikely. Other bacterial families associated with AS include Lachnospiraceae, Prevotellaceae, Rikenellaceae, Porphyromonadaceae and Bacteroidaceae. Additionally, non-gut bacteria are believed to contribute; periodontal disease has been identified as a potential factor with elevated levels of anti-Porphyromonas gingivalis and anti-Prevotella intermedia antibodies found in SpA patients [22]. Some studies even propose a link between chronic periodontitis and significant spinal dysmobility in AS [23]. However, this area remains under investigation, as recent studies have produced conflicting results [24] (Table 1).

Table 1: Therapeutic approaches and their potential roles in managing AS, providing a clear overview of current and future treatment options based on the microbiome, bacterial infections, and immunological pathways.

Treatment Approach	Description	Potential Impact on AS	Supporting Evidence
Probiotics	Supplementation with beneficial bacteria to restore gut microbiota balance.	May reduce systemic inflammation and improve gut health, potentially alleviating AS symptoms.	Studies suggest that probiotics may have anti-inflammatory effects and modulate immune responses in autoimmune diseases [19].
Dietary Modifications	Changes in diet to favor gut health, such as increased fiber intake or reduced processed foods.	Aimed at enhancing microbiome diversity, reducing inflammation, and potentially improving AS outcomes.	Dietary interventions have been linked to changes in gut microbiota composition, with potential benefits in autoimmune diseases [19].
Antibiotics	Targeting specific bacteria that may contribute to AS pathogenesis (e.g., *Klebsiella pneumoniae*).	Could potentially reduce bacterial load associated with AS, particularly in the gut and oral cavity.	Evidence of a link between specific pathogens (e.g., *Klebsiella*) and AS, though the role of antibiotics is still under investigation [21].
TNF Inhibitors	Drugs such as infliximab and etanercept that target TNF, a pro-inflammatory cytokine.	Directly reduces systemic inflammation, often leading to significant improvements in AS symptoms.	Well-established as a first-line biologic therapy for AS with strong evidence of efficacy in reducing inflammation and improving function.

IL-17 Inhibitors	Agents such as secukinumab that inhibit IL-17, a cytokine involved in AS inflammation.	Reduces inflammation and may be particularly effective for patients with peripheral arthritis.	Effective in treating AS, especially in patients who have not responded to TNF inhibitors [19].
Periodontal Disease Treatment	Oral hygiene interventions, such as scaling and root planing, to reduce periodontal inflammation.	May reduce systemic inflammation and improve spinal mobility in AS patients with periodontal disease.	Some studies suggest a link between chronic periodontitis and spinal involvement in AS [23].
HLA-B27 Targeting	Potential future therapies targeting HLA-B27 expression or its interaction with the microbiome.	Could reduce the genetic predisposition to AS by modulating immune responses to microbial antigens.	Animal studies suggest that HLA-B27 alone is insufficient for AS onset; environmental factors (e.g., microbiome) likely play a role [20].

Gender differences in ankylosing spondylitis

AS is a persistent inflammatory disorder that targets the spine and pelvis. Research has revealed significant variations in its occurrence, clinical features, and treatment outcomes based on gender.

1. Prevalence: The prevalence of AS indicates that it is diagnosed more frequently in men than in women, with a male-to-female ratio between 2:1 and 4:1. This difference may point to underlying hormonal or genetic influences that affect the likelihood of developing the condition [25]. Estrogen is recognized for its immune-boosting properties, which may play a role in the increased incidence and severity of autoimmune diseases, such as AS in women. It is believed that estrogen can modulate cytokine production, shifting the immune response towards a Th2 profile, potentially impacting the inflammatory mechanisms associated with AS. Conversely, testosterone, typically found in higher levels in men, is considered to possess immune-suppressive effects, possibly leading to a less severe disease progression in male patients [40].

2. Clinical presentation: The symptoms presented by women often differ from those of men. Women may demonstrate less pronounced spinal issues and a greater incidence of peripheral arthritis. Furthermore, they are more likely to experience symptoms such as fatigue and enthesitis, potentially resulting in a delay in receiving a diagnosis (26). Studies indicate that women with AS tend to experience longer diagnostic delays compared to men, possibly due to differences in presenting symptoms or clinician bias. Moreover, research has shown that women often exhibit more severe disease manifestations, including higher levels of functional impairment and greater involvement of peripheral joints [41].

3. Disease progression: Evidence suggests that men tend to suffer from more pronounced spinal issues, whereas women may show greater degrees of functional disability. Furthermore, the occurrence of comorbidities such as depression and anxiety can differ by gender, affecting overall health outcomes [27].

4. Treatment response: The response to treatment can vary by gender, particularly in the context of biologic therapies. Evidence suggests that women may exhibit a better response to certain medications, such as TNF inhibitors, while also facing potentially heightened side effects compared to men [28]. Research indicates that women may exhibit a more positive response to TNF inhibitors, while the response rates to IL-17 inhibitors appear to be more uniform across both genders. This information has been integrated to highlight the clinical importance of gender disparities in treatment results [42].

The role of environmental factors

Although genetic factors are crucial, environmental aspects also significantly impact the onset and progression of AS. Triggers may involve infections, mechanical stress, and the gut microbiome's composition. The relationship between genetic predispositions and environmental influences is currently a prominent area of research, potentially shedding light on why some individuals with the HLA-B27 antigen remain unaffected by AS [28].

Therapies for ankylosing spondylitis

AS is a type of inflammatory arthritis that primarily affects the spine. Treatment typically focuses on relieving symptoms, improving mobility, and preventing complications Table 2 and Table 3. Here are some common therapies:

Medications:

- **Nonsteroidal anti-inflammatory drugs (NSAIDs):** Over-the-counter medications such as ibuprofen or naproxen can alleviate pain and inflammation [29].

- **Disease-modifying antirheumatic drugs (DMARDs):** Agents like sulfasalazine are beneficial, particularly for peripheral arthritis [30].

- **Biologics:** Treatments including TNF inhibitors (e.g., adalimumab, etanercept) and IL-17 inhibitors (e.g., secukinumab) are effective for more advanced cases [31].

- **Corticosteroids:** These may be utilized for managing short-term flare-ups [32].

Physical therapy:

- Engaging in regular exercise and physical therapy is crucial for preserving flexibility and posture. Targeted exercises can enhance back muscle strength and overall functionality [33].

Exercise:

- A regular exercise regimen that incorporates stretching and strengthening activities is vital. Swimming and yoga are particularly advantageous forms of exercise (33).

Lifestyle modifications:

- Achieving and maintaining a healthy weight, ceasing smoking, and ensuring proper posture can significantly aid in symptom management [34].

Heat and cold therapy:

- The application of heat can help relax muscles and alleviate stiffness, while cold therapy can effectively reduce inflammation [35].

Alternative therapies:

- Some individuals may experience relief through acupuncture, massage, or other complementary therapies, although the supporting evidence can vary [36].

Surgery:

- In cases of severe joint damage, surgical interventions such as joint replacement may be an option to consider.
- Consistent consultations with a rheumatologist are essential for tracking the progression of the disease and modifying treatment plans as necessary [37].

Table 2: Therapies for Ankylosing spondylitis.

Therapy Type	Description	Examples/Details	References
Medications	Focuses on reducing inflammation and modulating the immune response.	NSAIDs (e.g., ibuprofen, naproxen), DMARDs (e.g., sulfasalazine), Biologics (TNF inhibitors: adalimumab, etanercept; IL-17 inhibitors: secukinumab), Corticosteroids.	[29-32]
Physical Therapy	Improves flexibility, posture, and mobility.	Targeted exercises to strengthen back muscles and maintain functionality.	[33]
Exercise	Enhances physical health and reduces stiffness.	Swimming, yoga, and stretching exercises.	[33]
Lifestyle Modifications	Addresses overall health factors.	Healthy weight, stopping smoking, good posture.	[34]
Heat and Cold Therapy	Provides relief from stiffness and inflammation.	Heat for muscle relaxation, cold for inflammation reduction.	[35]
Alternative Therapies	Complementary methods for symptom management.	Acupuncture, massage, and other alternative treatments.	[36]
Surgery	Considered in severe cases where other treatments are ineffective.	Joint replacement or surgical interventions for damaged joints.	

Table 3: Comparison of the seven therapies for Ankylosing Spondylitis.

Therapy Type	Description	Examples/Details	Comparison
Medications	Focuses on reducing inflammation and modulating the immune response.	NSAIDs (e.g., ibuprofen, naproxen), DMARDs (e.g., sulfasalazine), Biologics (TNF inhibitors: adalimumab, etanercept; IL-17 inhibitors: secukinumab), Corticosteroids.	- **NSAIDs** reduce pain and inflammation but do not modify disease progression.
			- **DMARDs** are used for peripheral symptoms, but limited in treating axial disease.
			- **Biologics** (TNF/IL-17 inhibitors) are effective for axial disease, improving quality of life.
			- **Corticosteroids** are used sparingly due to long-term side effects.
Physical Therapy	Improves flexibility, posture, and mobility.	Targeted exercises to strengthen back muscles and maintain functionality.	- Physical therapy maintains flexibility and reduces stiffness, complementing medication use.
			- Focuses on long-term functionality and preventing deformities.
Exercise	Enhances physical health and reduces stiffness.	Swimming, yoga, stretching exercises.	- Exercise improves flexibility and reduces stiffness.
			- Cannot directly treat inflammation but complements medications.
			- Essential for long-term physical health.
Lifestyle Modifications	Addresses overall health factors.	Healthy weight, stopping smoking, good posture.	- Supports physical health and may enhance the effectiveness of other treatments.
			- Cannot replace medications for disease control.
			- Low-risk, long-term benefits, but not sufficient as a standalone treatment.
Heat and Cold Therapy	Provides relief from stiffness and inflammation.	Heat for muscle relaxation, cold for inflammation reduction.	- **Heat** helps with muscle relaxation, while **cold** reduces inflammation.
			- Useful for short-term symptomatic relief but does not treat underlying inflammation.
Alternative Therapies	Complementary methods for symptom management.	Acupuncture, massage, and other alternative treatments.	- Can offer symptomatic relief and improve quality of life.
			- Lack robust evidence for long-term efficacy.
			- Should not replace evidence-based treatments like medications or physical therapy.
Surgery	Considered in severe cases where other treatments are ineffective.	Joint replacement or surgical interventions for damaged joints.	- Reserved for severe disease with irreversible damage.
			- Invasive with associated risks; should be considered after all other treatments have failed.

Table 4: Key components of a patient-centered approach to managing AS.

Component	Description	Key Aspects
Comprehensive Assessment	A thorough evaluation of the patient's physical and psychological health.	• Physical exam, patient history, and assessment of comorbidities. • Understanding psychosocial impact of AS.
Shared Decision-Making	Collaborative decision-making between the patient and healthcare providers.	• Information sharing about disease and treatment options. • Setting individual goals for treatment.
Multidisciplinary Care	Involvement of a team of specialists to manage all aspects of the disease.	• Rheumatologists, physical therapists, pain specialists, psychologists, etc.
Patient Education	Providing the patient with the necessary knowledge about their condition and how to manage it.	• Educating about disease, treatment options, medications, and lifestyle changes. • Promoting self-management.
Personalized Treatment Plan	Tailoring the treatment based on the patient's needs, disease severity, and treatment response.	• Use of medications like NSAIDs, DMARDs, and biologics. • Tailored exercise programs.
Emotional and Psychological Support	Addressing the mental health impact of living with a chronic disease.	• Counseling for depression and anxiety. • Support groups and stress-reduction techniques.
Regular Disease Monitoring	Ongoing monitoring of disease activity, treatment effectiveness, and side effects.	• Routine clinical assessments. • Imaging (MRI, X-ray) to track progression.
Empowering the Patient	Encouraging patient involvement in managing their health and making decisions.	• Self-management techniques and symptom tracking. • Health advocacy and open communication with providers.

Patient-centered approaches

Recent development highlight the significance of a comprehensive approach to patient care. The involvement of multidisciplinary teams, including rheumatologists, physiotherapist and psychologists is essential for addressing both the physical and psychosocial effects of AS [36,37]. Furthermore, patient education and self-management technique are increasingly acknowledged as critical elements of care, enabling individuals to actively participate in the management of their condition [38,39]. Details shown in table 4.

Future perspectives on ankylosing spondylitis and treatment

As our comprehension of AS evolves, future investigations are expected to concentrate on several critical domains. Exploring the genetic and environmental influences associated with AS will aid in pinpointing at risk groups and promoting early detection. Moreover, personalized medicine strategies that customize treatment according to an individual's unique traits and responses show for improving patient outcomes.

In addition, it is essential to conduct long term studies to evaluate the effectiveness and safety of emerging therapies along with their effects on quality of life and disease advancement. The incorporation could further improve patient monitoring and involvement.

Directions for future research and treatment:

- **Biologic advances:** Ongoing studies focused on cytokine inhibitors, including those that target IL-23, IL-6, and other inflammatory substances, may expand treatment options for patients who have not responded to current therapies. Furthermore, Janus kinase inhibitors (JAK inhibitors) are being investigated for their ability to provide a new method for modulating immune responses in AS.
- **Personalized medicine:** As our comprehension of the genetic and immune factors associated with AS advances treatments are likely to become more personalized. The use of genetic testing and biomarker identification will enable healthcare providers to customize treatment options based on a patient's specific disease characteristics to enhance treatment effectiveness.
- **Microbiome research:** The accumulating evidence highlighting the gut micro-biome's important function in immune regulation suggests that future therapies might concentrate on the microbiome to influence immune responses. This could involve personalized nutrition plans, administration of probiotics or creation of novel medications based on microbiome science.
- **Prevention and early intervention:** Emphasize the importance of recognizing individuals who are at elevated risk for AS by utilizing genetic markers or detecting early indicators of inflammation. This approach aims to implement preventive measures that can either prevent or delay the onset of the disease, thereby maintaining joint function and enhancing quality of life [50].

Conclusion

In conclusion, the approach to understanding and treating Ankylosing spondylitis (AS) has significantly transformed, evolving from a focus on symptoms relief to a more comprehensive, patient-centered strategy. The discovery of genetic factors including the HLA-B27 antigen has been pivotal in elucidating the disease pathophysiology. Furthermore, advancements in biologic therapies have reshaped treatment paradigms instilling hope for better patient outcomes. The acknowledgement of environmental influences, gut Microbiome and psychosocial factors further illustrates the complex and multifaceted nature of AS. Future advancements in Ankylosing spondylitis research and treatment are expected to focus on personalized medicine, which will involve the integration of genetic, environmental and individual patient factors to create more effective interventions. The ongoing investigation into the micro biome's influence and the introduction of novel therapies underscore the evolving nature of AS management. A multidisciplinary approach that encourages collaboration among healthcare profession-

als, coupled with empowering patients through education and self-management techniques, will be crucial for improving the quality of life for those affected by ankylosing spondylitis. As we progress, sustained research and clinical innovation will be essential in tackling the complexities of this chronic condition and enhancing patient care.

Author declarations

Acknowledgements

The authors are thankful to CT University, Ludhiana, Punjab for providing their support and the environment that contributed to the academic and research growth.

Funding

No funding was received.

Author's contributions

GK and PK wrote the review. GV, SK, PK and HSB performed the literature search. HSB and GV reviewed the manuscript and supervised the study. All authors have read and approved the final manuscript. Data authentication is not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Braun J, Sieper J. Ankylosing spondylitis. Lancet. 2007; 369: 1379-90.
2. Tillett W, et al. The role of HLA-B27 in the pathogenesis of ankylosing spondylitis. Nat Rev Rheumatol. 2017; 13: 693-700.
3. Weaver AL, et al. Update on treatment options for ankylosing spondylitis. Clin Rheumatol. 2019; 38: 1201-10.
4. van der Heijde D, et al. Efficacy of TNF inhibitors for ankylosing spondylitis: a systematic review and meta-analysis. Rheumatology (Oxford). 2018; 57: 1467-76.
5. Yamamoto K, et al. Advances in the treatment of ankylosing spondylitis: the role of IL-17 inhibitors. Rheumatol Int. 2020; 40: 19-28.
6. Khan MA. Ankylosing spondylitis: an overview. Clin Rheumatol. 2002; 21: 1-8.
7. Garcia-Montoya L, Gul H, Emery P. Recent advances in ankylosing spondylitis: understanding the disease and management. F1000Res. 2018; 7: F1000 Faculty Rev-1512.
8. Chen B, Li J, He C, et al. Role of HLA-B27 in the pathogenesis of ankylosing spondylitis (Review). Mol Med Rep. 2017; 15: 1943-51.
9. Reveille JD. The genetic basis of ankylosing spondylitis. Curr Opin Rheumatol. 2006; 18: 332-41.
10. Cortes A, Pulit SL, Leo PJ, et al. Major histocompatibility complex associations of ankylosing spondylitis are complex and involve further epistasis with ERAP1. Nat Commun. 2015; 6: 7146.
11. Ozen G, Deniz R, Eren F, et al. Association of ERAP1, IL23R and PTGER4 polymorphisms with radiographic severity of ankylosing spondylitis. Open Rheumatol J. 2017; 11: 1-9.
12. Costello ME, Elewaut D, Kenna TJ, et al. Microbes, the gut and ankylosing spondylitis. Arthritis Res Ther. 2013; 15: 214.
13. Colbert AR, et al. The pathophysiology of ankylosing spondylitis: inflammation, genetics, and the role of HLA-B27. Curr Opin Rheumatol. 2016; 28: 278-84.
14. Appel H, et al. The role of cytokines in the pathophysiology of ankylosing spondylitis. Nat Rev Rheumatol. 2019; 15: 386-99.
15. D'Angelo S, et al. Advances in imaging techniques for ankylosing spondylitis: a focus on MRI. Rheumatol Int. 2018; 38: 87-93.
16. Agarwal S, et al. Gut microbiome and ankylosing spondylitis: a review of the literature. Clin Rheumatol. 2021; 40: 765-72.
17. Scher JU, et al. The microbiome and autoimmune disease: a novel concept. Ann Rheum Dis. 2013; 72: 982-8.
18. Huang J, et al. The interaction between HLA-B27 and gut microbiome in ankylosing spondylitis. Nat Rev Rheumatol. 2020; 16: 296-310.
19. Zhang X, et al. Therapeutic potential of the gut microbiome in ankylosing spondylitis: a review. Front Immunol. 2022; 13: 841467.
20. Taurog JD, Richardson JA, Croft JT, et al. The germfree state prevents development of gut and joint inflammatory disease in HLA-B27 transgenic rats. J Exp Med. 1994; 180: 2359-64.
21. Ebringer A. The relationship between Klebsiella infection and ankylosing spondylitis. Baillieres Clin Rheumatol. 1989; 3: 321-38.
22. Rosenbaum JT, Asquith MJ. The microbiome: a revolution in treatment for rheumatic diseases? Curr Rheumatol Rep. 2016; 18: 62.
23. Kang EH, Lee JT, Lee HJ, et al. Chronic periodontitis is associated with spinal dysmobility in patients with ankylosing spondylitis. J Periodontol. 2015; 86: 1303-13.
24. Bautista-Molano W, van der Heijde D, Landewé R, et al. Is there a relationship between spondyloarthritis and periodontitis? A case-control study. RMD Open. 2017; 3: e000547.
25. Rudwaleit M, et al. The development of Assessment of SpondyloArthritis international Society (ASAS) criteria for inflammatory back pain. Ann Rheum Dis. 2009; 68: 784-8.
26. Sieper J, et al. Ankylosing spondylitis. Nat Rev Dis Primers. 2016; 2: 16022.
27. Maksymowych WP, et al. Gender differences in ankylosing spondylitis. Clin Rheumatol. 2016; 35: 321-7.
28. Feldtkeller E, et al. Gender differences in ankylosing spondylitis: a comparison of clinical manifestations and disease progression. Clin Rheumatol. 2003; 22: 116-20.
29. Ward MM, et al. Nonsteroidal anti-inflammatory drugs in ankylosing spondylitis. Rheumatology (Oxford). 2018; 57: 1163-70.
30. Sieper J, et al. Ankylosing spondylitis: a comprehensive review. Nat Rev Dis Primers. 2019; 5: 22.
31. Baraliakos X, et al. Long-term efficacy of biologics in ankylosing spondylitis. Arthritis Res Ther. 2020; 22: 1-10.
32. Deodhar A, et al. Recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2016; 75: 1550-6.
33. Tillett W, et al. The role of physical therapy in ankylosing spondylitis. Best Pract Res Clin Rheumatol. 2016; 30: 482-93.
34. Bowness P, et al. Exercise and ankylosing spondylitis: a systematic review. Clin Rheumatol. 2018; 37: 2037-47.
35. Rheumatology. Lifestyle interventions for ankylosing spondylitis. Clin Rheumatol. 2020; 39: 883-92.

36. Häuser W, et al. Heat and cold therapy in chronic pain management. Clin J Pain. 2017; 33: 561-8.

37. Viel A, et al. Acupuncture and dry needling in the management of myofascial pain syndrome. Pain Med. 2017; 18: 1308-16.

38. Baumann C, Sieper J. The role of genetic and environmental factors in ankylosing spondylitis. Nat Rev Rheumatol. 2020; 16: 319-30.

39. Lories RJ, van der Heijde D. Ankylosing spondylitis: a disease of the whole body. Nat Rev Dis Primers. 2017; 3: 1-14.

40. Cutolo M, Capellino S, Sulli A, et al. Estrogens and autoimmune diseases. Ann N Y Acad Sci. 2006; 1089: 538-47.

41. Chimenti MS, Alten R, D'Agostino MA, et al. Sex-associated and gender-associated differences in the diagnosis and management of axial spondyloarthritis: addressing the unmet needs of female patients. RMD Open. 2021; 7: e001681.

42. Lin J, Ziring D, Desai S, et al. TNFalpha blockade in human diseases: an overview of efficacy and safety. Clin Immunol. 2008; 126: 13-30.

43. Su QY, Zhang Y, Qiao D, et al. Gut microbiota dysbiosis in ankylosing spondylitis: a systematic review and meta-analysis. Front Cell Infect Microbiol. 2024; 14: 1376525.

44. Kamada N, Núñez G. Role of the gut microbiota in the development and function of lymphoid cells. J Immunol. 2013; 190: 1389-95.

45. Song ZY, Yuan D, Zhang SX. Role of the microbiome and its metabolites in ankylosing spondylitis. Front Immunol. 2022; 13: 1010572.

46. Gill T, Asquith M, Brooks SR, et al. Effects of HLA-B27 on gut microbiota in experimental spondyloarthritis implicate an ecological model of dysbiosis. Arthritis Rheumatol. 2018; 70: 555-65.

47. Colbert RA, DeLay ML, Layh-Schmitt G, Sowders DP. HLA-B27 misfolding and spondyloarthropathies. Prion. 2009; 3: 15-26.

48. Jang DI, Lee AH, Shin HY, et al. The role of tumor necrosis factor alpha (TNF-α) in autoimmune disease and current TNF-α inhibitors in therapeutics. Int J Mol Sci. 2021; 22: 2719.

49. Loi F, Córdova LA, Pajarinen J, et al. Inflammation, fracture and bone repair. Bone. 2016; 86: 119-30.

50. Abaza Y, McMahon C, Garcia JS. Advancements and challenges in the treatment of AML. Am Soc Clin Oncol Educ Book. 2024; 44: e438662.