AYUSHDHARA
ISSN: 2393-9583 (P)/ 2393-9591 (O)
An International Journal of Research in AYUSH and Allied Systems

Review Article

THE INTERPLAY OF EPIGENETICS, GUT DYSBIOSIS, *AMA* AND *MANDAGNI* IN AUTOINFLAMMATORY PATHOGENESIS OF ANKYLOSING SPONDYLITIS - A SCIENTIFIC REVIEW

Anirban Singha[1]*, Reetu Sharma[2]
*[1]PG Scholar, [2]Associate Professor, Dept. of Roganidana evum Vikriti Vigyana, NIA, Jaipur, Rajasthan, India.

Article info
Article History:
Received: 19-01-2025
Accepted: 24-02-2025
Published: 20-03-2025
KEYWORDS:
Ama, Mandagni, Gut Dysbiosis, Ankylosing Spondylosis (AS).

ABSTRACT

Ankylosing Spondylitis (AS) is a chronic autoimmune disorder primarily affecting the spine and sacroiliac joints, often leading to progressive stiffness, pain, and structural damage. Despite advances in conventional treatment, existing therapies remain largely palliative, with no definitive cure. This review explores the pathogenesis of AS through the interplay of epigenetics, gut dysbiosis, and metabolic dysfunction, emphasizing their correlation with Ayurvedic concepts such as *Ama* and *Mandagni*. Emerging evidence suggests that gut microbiome imbalances contribute significantly to chronic inflammation in AS, promoting immune dysregulation through antigenic mimicry and intestinal barrier dysfunction. Ayurveda describes a similar mechanism wherein improper digestion leads to Ama formation, which, under the influence of *Mandagni*, penetrates systemic circulation and triggers inflammatory cascades. The review integrates modern and Ayurvedic perspectives, proposing that *Mandagni*, or metabolic hypofunction, is the underlying factor connecting gut dysbiosis, chronic inflammation, and immune dysfunction. Furthermore, epigenetic modifications influenced by diet, lifestyle, and environmental factors act as triggers in genetically predisposed individuals, aligning with the Ayurvedic notion of *Nidana* (causative factors). A comparative analysis of modern and Ayurvedic treatment modalities highlights the potential role of *Sopha* and *Vatavyadhi* management in addressing the root causes of AS. Therapeutic interventions such as dietary modifications, gut microbiome restoration, detoxification (*Shodhana*), and *Rasayana* therapy may provide a holistic approach to disease prevention and management.

INTRODUCTION

Ankylosing Spondylitis (AS), a form of Ankylosing Spondylosis, is an autoimmune disorder primarily affecting the spinal joints, sacroiliac joints (SIJs), and surrounding soft tissues, including tendons and ligaments. In advanced stages, persistent inflammation can lead to fibrosis and calcification, ultimately causing reduced flexibility and spinal fusion, creating a rigid, "bamboo-like" appearance.[1] A systematic review showed prevalence of AS in India to be between 7-9.8 per 10,000 population. [2] With an early age of onset generally in the mid-twenties, the course of AS can also result in many extraarticular manifestations. Both these factors correlate positively with a poor Quality of Life and increased disease burden in the patients of AS. The available medicinal and surgical treatment are only palliative in nature and there is no as such cure till date. As Ankylosing Spondylitis (AS) typically begins at a young age, its socioeconomic impact on both patients and society can be significant. Numerous studies have documented considerable work disability, though rates vary across different countries. Work withdrawal is more common among individuals diagnosed at an older age, those in manual labor, or those with lower educational levels. Meanwhile, in employed individuals, sick leave is primarily linked to disease activity and physical function. [3]

Access this article online	
Quick Response Code	
	https://doi.org/10.47070/ayushdhara.v12i1.1873

In this article we try to explore the role of gut dysbiosis and epigenetic factors in promoting the inflammatory onset of AS in the backdrop of *Mandagni.* We also try to rationalise a novel preventive and therapeutic approach for AS following the treatment principles of Sopha and *Vatavyadhi.*

MATERIALS AND METHOD

A search was conducted using PubMed and Google Scholar with search terms: AS, pathogenesis, treatment, *Vatavyadhi*, gut microbiome, *Ama* and *mandagni*. Both original research articles and review papers were selected for further analysis, covering literature from the earliest available records up to March 2023. A manual review of reference lists from relevant sources identified through database searches was also conducted. Literature deemed relevant was included for in-depth study. Additionally, several authoritative Ayurvedic textbooks were reviewed to present classical Ayurvedic theories.

RESULTS

Epigenetics as a Trigger for Autoinflammation- *Nija Sotha* (inflammation due to indigenous causes)

Anaya et al. comprehensively review the concept of "autoimmune ecology," which encompasses interactions between environmental factors, molecular mechanisms, and the immune system. They examine how microbiota, vaccines, lifestyle, socioeconomic status, organic solvents, and ultraviolet rays influence innate immunity. These factors interact through pathways such as toll-like receptor signaling, B-cell activation, T helper 17, and regulatory T cells, as well as posttranslational and epigenetic modifications. Their study synthesizes existing research on how the exposome shapes immune responses, potentially leading to autoimmune diseases. [4]

Ayurvedic classics suggest that repeated mistakes in daily routines disrupt physiological balance. Factors like chronic illness, improper medical treatments, and persistent poor digestion from unhealthy eating disturb *Tridosha*, ultimately leading to *Sotha* (inflammation). [5]

Gut Dysbiosis- The product of Hypometabolism

Research indicates that gut microflora, shaped by diet and digestion, plays a role in the pathways connecting diet to low-grade inflammation. In mice with colitis, fat depots exhibited elevated expression of inflammatory cytokines and the nuclear receptors PPARγ and FXR. [6] To date, altered gut microflora remains the sole biomarker connecting digestive health to inflammation. [7] In the opinion article by Saxena, probiotic treatment is proposed as an alternative to the conventional treatment of Guillain–Barré syndrome, an immune-mediated peripheral neuropathy. The main idea is that probiotics may help to normalize the dysbiosis microbiota and replenish Treg cells to promote immune homeostasis.[8] The severe metabolic dysfunction observed in autoimmune diseases stems from a shared underlying mechanism: the gradual accumulation of pathogens in the microbiome. These pathogens have the capacity to disrupt gene transcription, translation, and essential human metabolic processes, contributing to disease progression. Autoimmune diseases are more likely to be passed down through families due to the transmission of a familial microbiome rather than Mendelian inheritance of genetic abnormalities. [9]

Ama- The sustainer of the Autoinflammation

In Ayurveda, the byproducts of improper digestion are referred to as *Ama*. Over time, *Ama* becomes internalized under the influence of *Vata*. This process is further facilitated by various factors interacting at the gut mucosa–lumen interface, contributing to its absorption and systemic effects. Under normal circumstances, gut epithelium controls internalization of large antigenic molecules through an intestinal barrier function. This barrier includes physical diffusion barrier, regulated physiological and enzymatic barrier, and immunological barrier which are under neurohormonal control and can be affected by various mechanisms like stress and dietary intakes. A continuous epithelial cell layer interconnected with tight junctions restricts both transcellular and paracellular permeation of molecules, thus constituting the principal component of intestinal barrier. In addition, the epithelium exerts an important physiological defence by secretion of fluid and mucus, together with secretory IgA, into the lumen to dilute, wash away, and bind noxious substances [10]. A mechanism which operates to cause intestinal barrier dysfunction may be complex and may involve either of the barriers discussed and may be considered under the umbrella term *Mandagni*. A loosening at the mucosal tight junctions, besides direct cellular damages in response to stress or incompatible intakes, becomes one plausible mechanism through which ama can find a way to get internalized to the gut peripheral tissue. This tissue is invariably rich in lymphatics and gives a reason to Ayurvedic perception of ama migration to the places which are like kapha. When Ama is internalized toward the gut periphery, it encounters various local immune factors. This interaction triggers immune responses, leading to localized inflammation. While this process is essential for maintaining gut immunity, excessive or prolonged activation can disrupt the gut mucosal architecture and contribute to *Mandagni*. A large quantity of ama added with a substantial barrier dysfunction may give ama a

way to get absorbed through portal system. Once internalized through portal system, ama is exposed to various food-related antigens and to various indigenous proteins. Due to their complex structure, ama is presumed to have a cross-reactivity to various macromolecular proteins intrinsically available in the body, a phenomenon recently studied in reference to various dietary proteins and their antigenicity in autoimmune conditions. [11]

Several human studies have reported elevated levels of systemic inflammatory markers, such as high-sensitivity C-reactive protein (Hs-CRP), interleukin-6 (IL-6), and TNF-α, in individuals consuming low-fibre, high-fat diets. [12] A recent study involving healthy men and women revealed that the omega-6 to omega-3 fatty acid ratio exhibited the strongest positive correlation with elevated levels of multiple inflammatory markers. This finding suggests that the ratio may serve as a potential indicator of low-grade, chronic inflammation. [13] Such food which is Guru-Snigdha (high fat containing, heavy to digest) produces *Ama*. which in turn causes Chronic inflammation in gut.

Mandagni- the mediating undercurrent

Mandagni or the hypoactive metabolic state can manifest at gastrointestinal tract level through a reduction in independent or cumulative enzyme quantity secreted in response to the dietary intakes. Any such deficiency will lead to an inadequate transformation of dietary intake into the subsequent end products; the result will be the production of *ama*. A further quest into *Mandagni* gives us a clue that *Mandagni* itself is not limited to transiently reduced enzymatic secretions but simultaneously also involves the factors which cause a permanent deficit into the enzyme secretion mechanism. An important mechanism which may be involved in *Mandagni*-related features could be a gradual destruction of intestinal mucosal cells responsible for enzyme secretion and a poor intramural plexus response to dietary stimuli, leading to a neurohormonal mechanism for enzymatic secretions. In whatever way the ama is produced, due to its increased influx in the gut mucosa in reference to *Mandagni* -related epithelial changes, it makes the surrounding immune system exposed to various new antigens, a pathology which marks the beginning to various autoimmune disorders.

Apart from the gut metabolism, the *Mandagni* condition also extrapolates to an inappropriate cellular metabolism, which can be the cause of the continuous autoimmune inflammatory cellular responses occurring in various parts of the body simultaneously.

Liu et al. demonstrated a significant correlation between disease activity in Crohn's Disease (CD) and Ankylosing Spondylitis (AS). CD activity was assessed using the CD Activity Index, while AS activity was measured with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Additionally, they found that CD activity was significantly associated with functional disability in AS, as evaluated by the Bath Ankylosing Spondylitis Functional Index (BASFI). Clinically evident IBD is observed in 6%-14% of AS patients, which is significantly more frequent compared to the general population.

The complete clinical picture in AS

A comprehensive review by Arleevskaya et al. points out to mainly four factors that cause the onset and sustain autoimmune inflammatory arthropathies: (i) higher susceptibility to bacterial and viral infections; (ii) greater imbalance of immune system components; (iii) limited capability to control and resolve inflammation; and (iv) compromised interaction at the microorganism–immune system interface. Thus, the disease onset is driven by the combination of genetic and environmental factors. [14]

The symptoms generally start at mid-twenties, with dull pain felt deeply in the lower lumber or gluteal region, low back morning stiffness that improves with activity and returns following inactivity. Pain gradually becomes persistent and bilateral with Bony tenderness in costosternal junctions, spinous processes, iliac crests, greater trochanters etc., Hip and shoulder arthritis may be present. Chronic tissue inflammation and healing leads to Fibrous Ankylosis followed by Syndesmophyte formation. This at a later stage causes bony ankylosis, fusing the vertebral bones together.

It is seen that patients with IBD related AS and IBD related isolated sacroiliitis are HLA-B27 positive in about 25%-78% emphasising the underlying chronic inflammatory condition in the patients.

The primary goals of treating Ankylosing Spondylitis (AS) are to preserve spinal flexibility, maintain proper posture, alleviate symptoms, minimize functional limitations, and prevent complications. Pharmacological management primarily includes nonsteroidal anti-inflammatory drugs (NSAIDs) and TNF-α inhibitors (TNFi). Other treatment options include non-TNFi biologics like secukinumab, as well as methotrexate and sulfasalazine. [15] NSAIDs, particularly selective cyclooxygenase-2 inhibitors, are the first-line treatment for individuals with active Ankylosing Spondylitis (AS). However, continuous NSAID use has not demonstrated any clinical advantages over on-demand treatment. [16] However, individuals receiving continuous NSAID treatment have a higher prevalence of hypertension and depression.

Available scientific literature in Ayurveda provides ample proof of disease modification and/or remission of symptoms in many autoinflammatory disorders. Nithyashree CT. et.al. concludes that the sound understanding of *Samprapti* and *Dosa* involvement is essential. These are pivotal for proper implication of *Shodhana* (detoxification) and Shamana (palliative), which have an upper hand in providing promising results. [17]

DISCUSSION

Ayurveda presents a unique perspective on the initiation of disease, suggesting that the very factors responsible for maintaining health under normal conditions can, when disrupted, contribute to the onset of illness. This highlights a fundamental balance between health and disease, where the same elements play dual roles depending on their state and function. This proposal has a beautiful resemblance to the concept of eco-balancing where a definitive sum of one entity is found responsible for a sustainable eco-health and failing to which a population is presumed to suffer from a cascade of anomalies related directly or indirectly to the primary imbalance. It proves that a disease cannot be considered as a mere sequence of defective genetic and biochemical steps. Indeed, the links between inflammation, altered gut microbiome and AS suggest that even seemingly distinct diseases can arise from fundamental aberrations in metabolism, homeostasis, and immune function. Thus, the autoinflammatory enthesitis in AS can be attributed partly to bad genes and the rest to bad luck.

Table 1 compares the modern and ayurvedic concepts of AS. It highlights new molecular evidence which validates certain ayurvedic concepts of AS.

Table 1

Points of Comparison	Concept of AS in Western Medicine	Concept of AS according to Ayurveda	Evidence supporting Ayurvedic view of AS
***Hetu* perspective**	Gut-Synovial axis hypothesis: environmental factors, such as gut bacterial dysbiosis, along with host-related mechanisms, including the migration of activated gut-derived T cells and macrophages, may contribute to the onset of inflammation in genetically susceptible individuals. These factors can serve as triggers for inflammatory responses targeting both the gut and joint tissues. [18]	*Mandagni* or a state of improper metabolism is the subtle undercurrent of all pathology as per Ayurveda.	Metabolism- both in the gut and in the cellular level is an inherent quality control mechanism of the individual. Thus, the status of *Agni* determines and maintains the character of the microbiological ecosystem in the body.
	Genetic Predisposition: Ankylosing spondylitis exhibits a strong familial association, with a sibling recurrence risk ratio exceeding 52, and is highly heritable (h^2 > 90%). The condition is two to three times more common in men than in women, with men typically experiencing more severe symptoms. Over 80% of affected individuals carry the HLA-B 27 allele; however, only a small fraction (1–5%) of HLA-B*27 carriers develop the disease. This low occurrence among carriers suggests that additional non–HLA-B 27 genetic variants play a significant role in influencing disease susceptibility. [19]	Due to the influence of *Daiva* (past deeds or unknown factors) or due to *Svabhavika Karanas* (in which we can include all the probable theories or mechanism of initiating autoimmune reaction such as microbial, genetic, immunological) potentially paving way to imbalance or disequilibrium or disability to the *Sahaja Satmya*, there by the immune cells (leucocytes) lose the ability to identify self from non–self or foreign agents. [20]	While the synovium and intervertebral discs of a joint fall under *Matrija bhava*, the joint and bone cartilage itself are *Pitrija Bhava*. Again, the *Kalaja* and *Yuktikrita Bala* will have their own share of influence. So, it's evident that certain components of bone and joint pathology can be inherited from both parents.
	The Epigenetic Trigger The role of genes in autoimmune diseases (ADs) is undeniable, with	Ayurveda considers a wide range of lifestyle related, diet related, iatrogenic, ante-natal,	The inflammatory response occurs in autoimmune disorders

	hundreds of risk loci identified, many of which are shared across different conditions. However, despite these genetic associations, a significant portion of heritability remains unexplained. The incomplete understanding of AD heritability suggests that genetic factors do not function in isolation but rather interact with environmental influences, highlighting the complex gene–environment interplay in disease development. [22]	post-natal factors as cause of beginning of inflammation. [21]	triggered by *Ama* or antigen at cellular level. Antigen vitiated *Dosha*, alters the immune response which can be considered as autoimmune diseases.
***Linga* perspective**	Morning stiffness along with dull and irregular pain marks the onset of autoinflammation. Tissue damage occurs as an indirect effect of the inflammatory process.	Initial symptoms of AS appearing as presentation of *Sopha*.	*Gatraguruta, Stambha* in all *Sandhiasthi* and *Parvapradesha*, restricted movements (reduced range of movement) Su Ni 1/39
	Persistent pain and bony tenderness develop. The buildup of leukocytes in the synovium is not due to local cell proliferation but rather results from their migration from distant sites of origin. This process is driven by the activation of synovial microvascular endothelial cells, which express adhesion molecules and chemokines that attract leukocytes to the inflamed tissue.	The ongoing sopha causes *Avarana* of *bahya Sira*, thus restricting the '*Avyahata gati*" of *Vayu*.	*Kaphavrita Vyanavata* leads to the manifestation of the conditions with multiple inflammatory lesions involving joints and restricts the movements.
	Chronic longstanding Inflammation leads to fibrous ankylosis followed by bony ankylosis	*Stambha, Sankoch, Bheda* and more severe forms of disabilities occurring.	Normal functioning of *Vata* hampered and manifestation of *Vatavyadhi* takes place due to *Margavarana.*
	Antigen/*Ama* modulates signalling at cellular levels leading to incompatible autoimmune response that damage tissues. Ankylosing spondylitis, Crohn's disease, psoriasis, rheumatoid arthritis, ulcerative colitis, and lupus erythematosus, - co-existence of two or more are seen in many advanced cases.	Arises as response against *Ama* or antigen[23]	*Asanjata Balapurusha* after recovery from a *vyadhi* becoming prone to develop inflammation. [24]
***Ausadha* perspective**	TNF-i is used with limited success to contain the inflammatory pathway.	*Laghvasana* (less food intake or food that takes less time to get digested) and *Langhana* (fasting).	A re-correction of *Agni* here essentially involves an architectural correction of intestinal mucosa which is ultimately responsible for the enzyme secretions. We are aware

			that intestinal mucosa observes a regular shedding off phenomena with its renewal at regular intervals. By avoiding the mechanisms which may be involved in gut mucosal destruction and by adopting a supportive mechanism to protect gut mucosal lining, a restoration of gut mucosa and subsequently *Agni* may be approached.
	Use of DMARD's in a hope to alter disease progression	The herbs rich in *Katu* (bitter), *Tikta* (pungent taste), and *Lavana* (salt) *Rasa* (taste) are found good to offer dissociative effects to ama. Ayurvedic formulations offering *Dipana* (ignition) and *Pachana* (dissociation) effects are mainly composed of components which are predominant in these *Rasas*.	A dissociation of the macromolecular structures of *Ama* into smaller fractions which independently may not have the adherence property of *Ama* is commonly employed approach of Ayurveda to dismantle internalized macromolecular *Ama*.
	Use of specific NSAID's give symptomatic relief	*Vatahara* drugs along with *Rasayana* therapy	Correction of the vitiated *Vata* along with attempt to rejuvenate the damaged tissues.

It is increasingly being recognized that there is a very close link between Inflammatory Bowel Diseases and Spondylo Arthropathies. There are multiple indications supporting this, including epidemiological, clinical, laboratory findings (such as HLA-B27 positivity), as well as histopathological and pathogenetic evidence. [25] The presence of a low grade chronic intestinal inflammation in patients of spondyloarthropathy only reiterates the role of *Mandagni* in sustaining the autoinflammatory mechanism in AS. The onset and continuation of inflammation in autoimmune diseases rely on the favourable presence and the maintenance of the 'perfect environment' or 'autoimmune ecosystem' within the host. Correction of the *Mandagni* can check the development of any pathognomic gut microbiota as well as cellular autoimmune reactions causing tissue damage at the level of Intervertebral discs.

From the discussion above, it is evident that AS presents mainly in two distinct clinical presentation- initially symptoms occur due to active Inflammatory phase. Later, as continuous tissue damage occurs due to Inflammation, pathogenesis of *Vatavyadhi* sets in due to *Dhatukshaya* and *Margavarana*. As *Vatavyadhi* sets in, the presentation may change accordingly as per site and predisposing factors[26] like enthesitis, anterior uveitis. Once a full-blown clinical picture of *Vatavyadhi* sets in, both textual references and therapeutic experiences suggest that, complete reversal to homeostasis is quite challenging if not impossible.

A novel therapeutic strategy in AS can thus be to identify the condition in the stage of *Sopha* itself and arrest any further disease progression by addressing the specific *Nidana* which can be the epigenetic triggers of the Autoimmune inflammation. Further studies are needed to thoroughly identify the probable wide spectrum of *Aharaja-Viharaja Nidana* that promotes manifestation of *Sopha* in AS.

Radiologic distinction to identify the two different stages of AS by Observational studies can be of landmark importance in this field. Also, associating any specific gut microbiome signature with AS can be

of tremendous value to assess disease response to *Sophahara* drugs in initial stages of AS.

In advanced stages of AS, where evidence of *Dhatukshaya* and debility is seen, besides *Vatahara* treatment, focus should be on rejuvenation of body tissues through *Rasayana* therapy. With the understanding of these new factors, the focus of treatment should be shifted to reversing the Autoimmune pathology rather than mere suppression of symptoms.

REFERENCES

1. Zhu, W., He, X., Cheng, K. et al. Ankylosing spondylitis: etiology, pathogenesis, and treatments. Bone Res 7, 22 (2019). https:// doi.org/10.1038/s41413-019-0057-8
2. Dean LE, Jones GT, MacDonald AG, Downham C, Sturrock RD, Macfarlane GJ. Global prevalence of ankylosing spondylitis. Rheumatology (Oxford). 2014 Apr; 53(4): 650-7. doi: 10.1093/ rheumatology/ket387. Epub 2013 Dec 9. PMID: 24324212.
3. Boonen A. Socioeconomic consequences of ankylosing spondylitis. Clin Exp Rheumatol. 2002 Nov-Dec; 20(6 Suppl 28): S23-6. PMID: 12463442.
4. Anaya JM, Ramirez-Santana C, Alzate MA, Molano-Gonzalez N and Rojas-Villarraga A (2016) The Autoimmune Ecology. Front. Immunol. 7:139. doi: 10.3389/fimmu.2016.00139
5. Acharya YT, ed., Charaka Samhita of Agnivesha elaborated by Charaka and Drdhabala with Ayurveda Dipika commentary by Sri Chakrapanidatta, Cikitsasthana, 12th chapter, 5th-8th verse, Varanasi: Chaukhamba Surbharati Prakashan, 2014.
6. T. Varga, Z. Czimmerer, and L. Nagy, "PPARs are a unique set of fatty acid regulated transcription factors controlling both lipid metabolism and inflammation," Biochimica et Biophysica Acta, vol. 1812, no. 8, pp. 1007–1022, 2011.
7. L. Galland, "Intestinal toxicity: new approaches to an old problem," Alternative and Complementary Therapies, vol. 3, pp. 288–295, 1997.
8. Saxena A (2016) Probiotics as a Potential Alternative for Relieving Peripheral Neuropathies: a Case for Guillain-Barré Syndrome. Front. Microbiol. 6:1497. doi: 10.3389/fmicb.2015. 01497
9. Satav, D. D. G., Dhanvijay, D. S. V., & Vaidya, D. K. C. (n.d.). A Study on Autoimmune Diseases and Ayurveda. The Journal of Oriental Research Madras, [Vol. XCIII-XVI], 31–38. Retrieved March 27, 2025, from https: //www.researchgate.net/ publication/368667581_8_A_STUDY_ON_AUTOIM MUNE_DISEASES_AND_AYURVEDA
10. Soderholm JD, Perdue MH (2001) Stress and the gastrointestinal tract II. Stress and intestinal barrier function. Am J Physiol Gastrointest Liver Physiol 280: G7–G13
11. Hvatum M, Kanerud L, Hallgren R, Brandtzaeg P (2006) The gut joint axis: cross reactive food antibodies in rheumatoid arthritis. Gut 55: 1240–1247
12. L. Galland, "Diet and inflammation," Nutrition in Clinical Practice, vol. 25, no. 6, pp. 634–640, 2010.
13. N. Kalogeropoulos, D. B. Panagiotakos, C. Pitsavos et al., "Unsaturated fatty acids are inversely associated and n-6/n-3 ratios are positively related to inflammation and coagulation markers in plasma of apparently healthy adults," Clinica Chimica Acta, vol. 411, no. 7-8, pp. 584–591, 2010.
14. Arleevskaya MI, Kravtsova OA, Lemerle J, Renaudineau Y and Tsibulkin AP (2016) How Rheumatoid Arthritis Can Result from Provocation of the Immune System by Microorganisms and Viruses. Front. Microbiol. 7:1296. doi: 10.3389/fmicb.2016.01296
15. Zhu, W., He, X., Cheng, K. et al. Ankylosing spondylitis: etiology, pathogenesis, and treatments. Bone Res 7, 22 (2019). https:// doi.org/10.1038/s41413-019-0057-8
16. ieper, J. et al. Effect of continuous versus on-demand treatment of ankylosing spondylitis with diclofenac over 2 years on radiographic progression of the spine: results from a randomised multicentre trial (ENRADAS). Ann. Rheum. Dis. 75, 1438–1443 (2016).
17. Nithyashree CT, Sujathamma K. Anterior Uveitis and management in Ayurveda - A Case Study. J Ayurveda Integr Med Sci 2017; 5: 206 210. http://dx.doi.org/10.21760/jaims.v2i05.10281
18. Arvikar SL, Fisher MC. Inflammatory bowel disease associated arthropathy. Curr Rev Musculoskelet Med. 2011; 4: 123–131.
19. International Genetics of Ankylosing Spondylitis Consortium (IGAS) et al. "Identification of multiple risk variants for ankylosing spondylitis through high-density genotyping of immune-related loci." Nature genetics vol. 45,7 (2013): 730-8. doi:10.1038/ng.2667
20. R. Nithin Krishnan, Nandesh Mohan. Concept of Vyadhikshamatva with special reference to Immune tolerance and Auto-Immunity. J Ayurveda Integr Med Sci 2016; 1(1): 68-72. http://dx.doi. org/10.21760/jaims.v1i1.3639

21. Anaya JM, Ramirez-Santana C, Alzate MA, Molano-Gonzalez N, Rojas-Villarraga A. The Autoimmune Ecology. Front Immunol. 2016 Apr 26; 7: 139. doi: 10.3389/fimmu.2016.00139. PMID: 27199979; PMCID: PMC4844615.
22. Acharya YT, ed., Charaka Samhita of Agnivesha elaborated by Charaka and Drdhabala with Ayurveda Dipika commentary by Sri Chakrapanidatta, Sutrasthana, 18th chapter, 6th verse, Varanasi: Chaukhamba Surbharati Prakashan.
23. Yadav PV, Medical Perspective on Ama as per Ayurveda and Modern Consideration: A Review, Journal of Drug Delivery and Therapeutics. 2020; 10(1-s): 205-207 http://dx.doi.org/10.22270/jddt.v10i1-s.3861
24. Dougados M, Soubrier M, Antunez A, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). Ann Rheum Dis. 2014; 73(1): 62-68.
25. Fragoulis GE, Liava C, Daoussis D, Akriviadis E, Garyfallos A, Dimitroulas T. Inflammatory bowel diseases and spondyloarthropathies: From pathogenesis to treatment. World J Gastroenterol 2019; 25(18): 2162-2176 [PMID: 31143068 DOI: 10.3748/wjg.v25.i18.2162]
26. Madhava Nidana, (Madhukosha) Madhavakar, revised by Vijayarakshita and Kanthadatta Madhukosha commentary and Vidyotini Hindi commentary by Ayurvedacharya Shri Susarshana Shastri, Edited by Ayurvedacharya Shri Yadunandana Upadhyaya, published by Chaukhamba Publications, 22nd Chapter 9th Verse, New Delhi, Edition 32, Year of reprint 2002.

Cite this article as:
Anirban Singha, Reetu Sharma. The interplay of Epigenetics, Gut Dysbiosis, Ama and Mandagni in Autoinflammatory pathogenesis of Ankylosing Spondylitis - a Scientific Review. AYUSHDHARA, 2025;12(1):364-371.
https://doi.org/10.47070/ayushdhara.v12i1.1873
Source of support: Nil, Conflict of interest: None Declared

***Address for correspondence**
Dr. Anirban Singha
PG Scholar,
Dept. of Roganidana evum Vikriti Vigyana, NIA, Jaipur
Email: thesingha24@gmail.com