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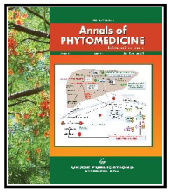

Review Article : Open Access

Exploring the interface between autoimmune diseases and Ayurveda: A comprehensive review

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Abstract

Autoimmune diseases are condition in which our own cells are being attacked by the immune system instead of protecting the body from foreign bodies. There are more than eighty autoimmune diseases which are found in human body. Some autoimmune diseases are more common which cause real hurdles to human. Compared to males, females are more commonly exposed to the disease, though it affects both genders irrespective of age, sex and race. Early diagnosis of these autoimmune disorders can help in preventing the bodily damage. Modern aspect clearly says that all autoimmune diseases are manageable, though it has unknown causes. But, Ayurveda is a unique system of medicine which totally differs from modern medicine. Ayurvedic science deals with physical and mental wellness. There are many techniques which are mentioned in Ayurvedic classical text books (Samhitas), to analyse the patient condition. Studying all kinds of autoimmune diseases through Ayurveda is challenging. The aim of this review article is to help to understand the disease nature, with the help of modern science, in order to treat the disease using Ayurvedic method.

1. Introduction

Healthy immune system fights with the disease and helps to attain wellness. There are more than eighty kinds of autoimmune diseases found in human body, with different pathology. Autoimmune disease is a condition in which our cells or organ is attacked by our own immune mechanism. Autoimmune disease can affect any part of the body or entire body parts easily, which depends on the nature of disease manifested in our body and can leads to life threatening situations. The disease on becoming chronic, makes a person disable so that the person can be depressed easily, which affects their lifestyle, families socio economic status. All autoimmune diseases require treatment immediately and continuously, otherwise it becomes a burden to patient and their family to run the normal life. Majority of autoimmune diseases have unknown cause but can be identified by signs and symptoms exhibited by the person and through diagnostic blood test. So, much of prospective studies are going to rule out the factors all over the world. At present, peoples are more prone to autoimmune diseases and the prevalence is increasing throughout the world, especially in developing and developed countries. The commonest autoimmune diseases are type 1 diabetes, which is a metabolic disorder, rheumatoid arthritis which is a musculoskeletal disorder, hashmotos thyroiditis which is an endocrine disorder. The most common neurodegenerative disorder is amyotrophic lateral sclerosis (Harsha *et al*., 2023).

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Ayurveda is the science which deals with all aspects of wellbeing of human. The main aim of Ayurveda is to protect the person from disease and cure the sick. There is evidence in Ayurvedic text books that immunity fights against all kinds of diseases. All diseases can be classified into four; namely, easily curable, curable with difficulty, manageable and incurable. All these are based on immune system. According to Ayurveda, autoimmune disease continuously involve unhealthy diet and activities. Byproduct from impaired process of digestion (Ama), is a concept, which hampers all the functions of body easily leading to the genesis of autoimmune diseases.

In Ayurveda, there is no manifestation of disease without causative factor. Every disease has its own causes, signs and symptoms, classification, pathogenesis and complication. Diagnostic procedure (Nidanapanchaka) are the prime tools to understand the disease in all aspects, which helps to treat the patient by palliative medicine. Most of the autoimmune diseases can be correlated based on causative factor (Nidana), signs and symptoms (Rupa) and pathogenesis of disease (Samprapti). The majority signs and symptoms of autoimmune diseases are mentioned in Ayurveda with different names such as anemia (Pandu), skin diseases (Kushta), diabetic mellitus (Prameha), goiter (Galaganda), disease of bone marrow (Majjavahasrotas), rheumatoid arthritis (Amavata), gouty arthritis (Vatarakta) and irritable bowel syndrome (Grahani) which is a very broad spectrum of diseases which can be correlated to most of the autoimmune diseases. This review article helps to shed light on various autoimmune diseases by understanding the causes, prevalence, types, investigation and prevention, along with Ayurvedic correlation, for providing better treatment purpose and for various research approaches. Here, we will look into common autoimmune diseases which occur frequently, its prevalence in recent

era and its types which is listed below briefly (Table 1). It also aims to address the challenges of transitioning pediatric patients to adult care and the need for specialized programs (Sagarkumar *et al*., 2023).

Table 1: Shows the different common autoimmune disease name, prevalence in recent era and types

S.No.	Disease	Prevalence	Types
1.	Rheumatoid arthritis	The world widely prevalence is approximately 0.5% to 1% among adults (Rohini *et al*., 2015)	Two main types in adults:Seropositive, seronegative and juvenile
2.	Type 1 diabetes	India has three new cases diagnosed daily 0-14 years (Ashok *et al*., 2015)	Type 1
3.	Psoriatic arthritis	Prevalence of psoriatic arthritis in India is 8.7 per cent in study period of one year (Sunil *et al*., 2014)	Five types distal interphalangeal predominant, asymmetric oligoarticular, symmetric polyarthritis, spondylitis and arthritis mutitans
4.	Hashimoto's thyroiditis	The prevalence of hashimoto's thyroiditis is one in 10 adults in the study population. Females are more prone (Sanjay *et al*., 2013)	Hypothyroid
5.	Graves disease	About 42 million people are suffering from Graves disease in India (Ambika and Usha, 2011)	Hyperthyroid
6.	Systemic lupus erythematosus	In India the prevalence of systemic lupus erythematosus ranges low from 14 to 60 per 100,000 (Malaviya *et al*., 1993)	Systemic and cutaneous lupus, neonatal and drug-induced lupus
7.	Psoriasis	Prevalence of psoriasis is 8 per cent in one year study period (Sunil *et al*., 2014)	Plaque, pustular, guttate, inverse and erythrodermic psoriasis
8.	Inflammatory bowel disease	Inflammatory bowel disease is increasing worldwide. There are around 6.8 million IBD cases recorded in 2017 year (Sabbu *et al*., 2023)	Crohn's disease and ulcerative colitis
9.	Sjogren's syndrome	Rarely reported in India	Primary and Secondary
10.	Multiple sclerosis	Prevalence rate of 5-20 per 100,000 (Rohit *et al*., 2015)	Primary and secondary progressive, relapsing remitting and finally progressive relapsing

2. Factors of autoimmune disease

2.1 Genetic

Genetic factors are involved much for the genesis of autoimmune diseases, which travels to next generation and produce the birth defects easily. Genetic predisposition involves a higher risk due to inherited gene variation. Genetic factors are divided into three groups, which are responsible for the manifestation of autoimmune diseases; namely, T cell receptors, immunoglobulins and the major histocompatibility complexes. The pathogenesis is multifactorial in autoimmune disease, which has been widely confirmed, and that there are several evidences available that the interaction between genetic and environmental factors is responsible for the development of autoimmunity (Costenbader *et al*., 2012a). The monozygotic twins and dizygotic twin's ratio are high concordance, which plays major role in the manifestation of autoimmune disease. There is a more recent study called genome, conducted by genome wide association, for identification of several genetic loci for susceptibility (Costenbader *et al*., 2012b). General genes are encoded when it is associated with proteins of immune, causing inflammatory autoimmune disease. Immune complexes including antigen, which comes under type I interferon, receptors and NF-κB signaling, functions of B-cell and T-cell, apoptosis and clearance of cellular components (Nagy *et al*., 2015a). Autoimmune diseases are diseases linked with protein variant. There is modification in genes, which represent the autoimmune disease, and it may be the same modification or others, which induce the autoimmune diseases in different way, in the body parts, resulting in the damage of the cells (Nagy *et al*., 2015b). Decoded genes are primarily responsible for human growth and development, from intrauterine life to other stages. There are features particular for growing hair pattern, skin structure, nail condition, eye structure and colour. When there is a threat, the genes attacks their own cells and it depends on the response of human genetics. Inherited disorders are primary immunodeficiency disorders and they occur at birth. Generation-to-generation, these genes pass down, which is a danger to control the manifestation of autoimmune disease. So, the diagnosis of these diseases should be done early or before birth. In certain cases, after birth, some of disease symptoms may not present itself and this can be delay diagnose of disease. In autoimmune conditions, evidence of a new genetic variation is found. Several genetic variations are emerging in recent era which is caused by food habits of human, which is against the nature. Autoimmune disorders have a complex genetic base in which multiple genes contribute to disease risk, each has independent modest effects. In addition, it is now clear that common genes underlie in multiple autoimmune disorders. There is also heterogeneity among sub phenotypes, within a disease and across major racial groups. Some biological factors are related to codon usage bias CUB (tRNA abundance, GC content, gene expression and gene length) (Manal *et al*., 2022). The segregated chromosomal linked within genetics of families is the phenotype. The segregated chromosomes are common for all autoimmune diseases. However, the genes are responsible for contribution of binding with antigen such as, NOD2 (nucleotide binding and

oligomerization domain 2) in Crohn's disease (CD) and more recently, STAT4 (signal transducer and activator of transcription 4) in rheumatoid arthritis (RA) and systemic lupus erythematosus.

2.2 Gene mapping

The gene studies helps to identify the location of chromosomes. The analyzing is based on association of genes. In some cases, gene patterns are wide and scanning. There is no evidences for mapping, but particular hypothesis is being addressed. The possibilities are there to discover the genome mapping. In this study, there is limitation in pathway to understand the autoimmune disease. Genes mapping methods are the only assumption criteria. Genomes wide association scanning has been proved effectively to study the gene mapping and chromosome location (Peter and Lina, 2009). Immunological mechanism is failure to initiate the disease of autoimmune. These mechanisms are as follows: polyclonal activation and self-reacting B-cells are generated to activate T suppressor and T increaser, both in fluctuation of anti-idio type network control. The antigen is released from the cells inheritably. Class II HLA antigens are released on the tissues at the time of autoimmune response. This could be the cause for increasing the familial incidence for many autoimmune diseases (Harshmohan, 2010a). The pathology of this antigen in immune dysregulation remains still under investigation. There is a chance that this is the gene variant in autoimmune diseases that pass to any children (Jorge *et al*., 2016).

2.3 Environment and sex factor

It has been identified that environmental factors indirectly impact the genes, when exposed to chronic predisposing genetic risk. But, unfortunately environmental factors are unavoidable for humans. One among the factor inherited to autoimmune disorder, is the environment and it also include the continuous changes in diet habits such as fast food, uncooked substance, *etc*. The reduced physical activity is one of the main causative factor for autoimmune diseases. Now, western culture implies to in society such conditions are increasing gradually in nation. Increasing incidence of autoimmune diseases and newly emerging diseases are directly caused by the environmental factors. Growing evidences suggest that, following a particular type of diet and activities related to human pathologies, can have a profound impact on local and systemic immune responses under physiological and autoimmune conditions, such as rheumatoid arthritis, graves disease and inflammatory bowel disease. Females are more prone to autoimmune diseases than males. This is because X chromosomes play a role for diseases process. Sex differences have a major role in the occurrence of autoimmune diseases. The documented are common in all disease. Two sex hormones are involved in the development of inflammatory autoimmune disease. Cytokine is a production chemical messenger responsible for pro-inflammatory and anti-inflammatory changes (Lasrado *et al*., 2020). In addition to the above factors, autoimmune diseases are governed by factors such as sex linked predilection, bacterial and viral infection and hormonal influences.

2.4 Microbial factors

Some microbial infections particularly viruses such as, Epstein-Barr virus infection and bacteria such as *Streptococci*, *Klebsiella* and *Mycoplasma* have found to be involved in pathology of autoimmune diseases (Harshmohan, 2010b). The humoral immune and cellular immune are involved in a response to any autoimmune disease. The humoral immune system is for the production of antibodies in an autoimmune disease and cellular immunity system is always responsible for the fight against the foreign bodies, through incompetent cells. The lymphocytes, macrophages, mitochondria, ribosomes and proliferation of T cells are responsible for the production of antibodies, and B cells produce only plasma cells for synthesizing the antibodies. On exposure to antigen, these synthesized antibodies interact with the antigen to form antigen antibody complexes. Auto immunity has less tolerance to autoantigens. Production of autoantibody is inherited in the normal immune system and it is called the feedback network of T and B cells. Mechanism of tissue damage is mainly of two types. Firstly, direct injury by autoantibody and secondly, the tissue damage occurs in body which is immune system complex mediated.

3. Classification of autoimmune disease

Autoimmune diseases can be classified by several criteria. It is mainly classified based on the location of the signs and symptoms produced and the system involved during the autoimmune attack. Based on this criteria, autoimmune diseases are system, organ and tissue involved. This classification pattern is useful for positioning the patients and for the primary response to physicians to treat the condition with a specialist.

3.1 Systemic

Systemic autoimmune diseases occur where auto antigen is found in the cells of body. DNA proteins which are complex, are found in all types of cells. Thus, the pathological damage has more chance of occurring in many cells, organs and tissues. Involved multiple organs and autoantibodies are directly against various structure of cells and tissue in non-organ specific, rheumatoid arthritis, myositis and connective tissue disease. Most common systemic diseases of autoimmune are: type 1 diabetes, psoriatic arthritis, rheumatoid arthritis and graves disease. These diseases are manageable by a rheumatic specialist. Autoimmune disease and rheumatism disease are often termed irremediable (Sagarkumar *et al*., 2023).

3.2 Organ specific

Autoimmune diseases affect specific organ or tissue, when a particular organ or tissue is targeted by the immune system of a person. For example, the thyroid gland in patients with graves disease, the beta cells of the endocrine pancreas in patients with type 1 diabetes, or the skin of a patient with vitiligo. In organ specific autoimmune diseases, the autoantibodies are directly acting against the specific organ. Hashimoto's thyroiditis, pernicious anemia, type 1 diabetes mellitus and various endocrinal disorders come under this group. But, in some cases, the patient might have both the autoantibodies, which is organ specific and nonspecific organ, in circulation. This happens only in chronic active condition of autoimmune. In such cases, the diseases arising are: hepatitis, myasthenia gravis, hemolytic anemia, thrombocytopenia by idiopathic and systemic lupus erythematosus, inflammatory process in allergy, rheumatic, metabolic disorders, arthritis, cardiovascular dysfunctions, liver disorder, colon disorder and cancerous changes (Rahul and Anita, 2023).

4. Pathogenesis of autoimmune disease

Pathology is the study about the disease manifestation involving organs, by various scientific methods. Hence, pathology can be defined as the scientific study of a disease. Diseases vary in different structure and may be defined as an abnormal variation in structure and function of the body parts. Four aspects to studying pathology of autoimmune diseases are: the etiology, pathogenesis, morphologic changes along with functional disarrangement and clinical significance. These four factors are the key to understand the pathogens of an infective autoimmune disease. Etiology means causative factors which are the triggering factors in the genesis of an autoimmune disease. The known cause of a disease is called the primary causative factors. When the cause of the disease is unknown, it is called idiopathic in medical science. Our aim is to rule out the primary cause, to subside the disease condition arising due to autoimmunity. It is challenging to find the prime causes. Once diagnosis is made, it can be understood that whether the diseases are treatable easily or not. There are two major etiologic factors: genetic and acquired in many disease including infectious, nutritional, chemical, physical, *etc*. The etiology is always the key for the pathogens in an autoimmune disease. The manifestation of pathogen in an organ could be during the incubation time. The incubation period is totally different in all infectious autoimmune diseases. So, the morphological changes in the cells also vary from cell-to-cell. The structural changes are identified by microscopic examination, by observing all the tissues microscopically. The identified morphologic changes are established as the clinical symptoms of an autoimmune condition. Functional disarrangement and its clinical significance along with the morphologic changes in the organ, influence the normal functioning of the organ. Understanding the histopathology of an autoimmune disease is useful in clinical correlation of the patient condition.

There are different diagnostic techniques we use in pathology, for accurate diagnosis. Mostly these diagnostic techniques are based on morphology and histopathology changes of the cells. The pathologist may use the following techniques to diagnose the diseases: a. histopathology, b. cytopathology, c. haematopathology, d. immunohistochemistry, e. microbiological examination, f. biochemical examination, g. cytogenetics, h. molecular techniques, i. autopsy.

5. The stages of autoimmune disease

Autoimmune diseases occurs in a short course of time. The existence of genetic, microbial, infectious and environmental factors are the sources for the causation of the genesis of an autoimmune diseases. The presence of genetic factors in the cells are primly responsible for disturbing the B cell and T cell signalling, which occurs in an early stage of life. After some time, the impact of these disturbances in cells are potentially connected with the infectious environment. There is an evidence that in women, sex hormones may enhances these cellular disturbances. Autoantibodies are elevated in autoimmune condition and the messenger of cytokines increases, which causes the disease to entering into a stages called asymptomatic or benign autoimmunity. This followed by the accumulation of other etiological factors, induces a transition to a stage of pre-clinical autoimmunity. Post-clinical autoimmunity represents the changes that occur after clinical recognition and initiation of therapy.

6. General signs and symptoms of autoimmune disease

Every autoimmune disease affects the person with different signs and symptoms, in different body parts, making the patient disable easily. Some signs and symptoms are more common to most of the autoimmune diseases which include redness of skin, inflammatory swelling, pain, fatigue, stomach ache, stiffness of joints, swollen glands, myalgia, muscle weakness, rashes, difficulty in breathing, recurring low grade fever, poor appetite, trouble concentrating, anxiety, numbness, mood swing, bloating and depression. These symptoms may vary based on disease pathology and the organ involved. The important symptoms of rheumatoid arthritis are the early symptoms like joint pain, swelling, tenderness, stiffness, fatigue and mild fever. Type 1 diabetes symptoms are polydipsia, polyphagia, unusual weight loss, blurred vision, fatigue, delay in healing of wounds, cuts and sores, vaginal infection and frequent urination. The symptoms of psoriatic arthritis include discoloration or pitting on the fingernails and toe nails, swelling in fingers and toes, bony pain and silver scaly patches on skin. Many patients remain asymptomatic, nevertheless, the hashmotosis disease can present with early symptoms, which may include difficulty in passing stool, fatigue, dry skin, increased in weight, and when progressed, the symptoms can be intolerance to cold, decreased energy, depression, loss of memory, hair loss, apnea, menorrhagia and hoarseness of voice. The signs and symptoms of graves disease include sweating, headache, unusual weight loss, nervousness, emotional disturbance, tremors, exophthalmos, arrhythmia, tachycardia, nausea, diarrhea and oligo menorrhea in female and muscle weakness. Systemic lupus erythematosus affects multiorgan and the symptoms are butterfly rashes and red patches in skin, endocarditis, atherosclerosis and fibrous sac inflammation in heart, blood in urine, pleuritic, pneumonitis, pulmonary emboli and pulmonary hemorrhage in lungs, mouth and nose ulcer, severe abdominal pain, anemia and swollen joints. In psoriatic condition, the symptoms are reddish inflamed patches on skin, whitish-silvery scales, dry skin, cracked skin and bleeding in patches, itchy and burning sensation in patches, and pitting in nails. Inflammatory bowel disease produce fever, night sweat, vomiting, fatigue, inflammation of eyes, sore, stomach pain, abdominal cramps, diarrhea, blood in stool, difficulty or incomplete bowel movements, irregular periods and weight loss. Sjogren's disease present with symptoms like prolonged fatigue, dry eyes, and sand like gritty sensation in mouth, dryness of vagina, skin rashes, joint swelling and pain, stiffness, tooth decay and gingivitis. Main signs and symptoms of multiple sclerosis are cognitive impairment, depression, anxiety, fatigue and unstable mood, nystagmus, optic neuritis and diplopia in vision dysarthria in speech, dysphagia in throat, weakness, spasms and ataxia in musculoskeletal system, incontinence, frequent and retention of urine, constipation and diarrhea, pain, hypoesthesia and paresthesia. It is clinically observed that some autoimmune diseases are inherited with another autoimmune disease.

7. Complications of autoimmune conditions

Autoimmune diseases can be complicated when the condition gets chronic. Some conditions are occur in all varieties of autoimmune diseases which include inflammation of heart disease, as a complication arising from rheumatoid arthritis and systemic lupus. Mood disorder such as depression and anxiety also arise due to

chronic condition of the illness. Rheumatoid arthritis and Sjögren's syndrome are caused by nerve damage called neuropathy. Deep vein thrombosis occurs in condition of ulcerative colitis and Crohn's disease. Autoimmune diseases if not treated timely, may lead to organ damage easily, *e.g*., uncontrolled diabetes mellitus may lead to renal failure.

8. Autoimmune disease with Ayurvedic correlation

All kind of autoimmune diseases can be ayurvedically correlated with the help of signs and symptoms easily. Rheumatoid arthritis can be correlated with disease rheumatism and the symptoms of the disease are pain all over the body (Angamardha), swelling in the joints (Shooniyathaanganam), heaviness of body (Gaurava), fever (Jwara) and fatigue (Alasya) (Srikantamurthy, 2009a). Type 1 diabetes can be correlated with diabetes (Prameha) disease, the main symptoms being increased quantity and turbidity of urine (Prabhootaavilamutrata) (Srikantamurthy, 2009b). Psoriatic arthritis comes under skin diseases (Ekakusta), the symptoms are, absence of perspiration (Asvedana), involvement of large area of skin (Mahavasthu) and skin resembling the scales of fish (Matsyashakalapam) (Srikantamurthy, 2009c). Hashimoto's thyroiditis disease can be correlated with disease of thyroid (Galaganda) and the symptoms are swelling in neck (Galaswayathu), mild pain (Mandharuja) and heaviness (Guru) (Srikantamurthy, 2009d). Graves disease also can be correlated to disease of thyroid (Galaganda), involving symptoms such as swelling in neck (Galaswayathu), pain (Toda) and dryness of throat and palate (Talugalashosha) (Srikantamurthy, 2009e). Systemic lupus erythematosus and Sjogren's syndrome can be correlated under the disease of arthritis (Vatarakta) and the symptoms are pain (Shoolam), swelling (Shota), pricking pain (Toda), tenderness in joints (Sparshaasahatvam), hot in touch (Ushma), inactivity (Staimitya) and numbness (Supti) (Srikantamurthy, 2009f). Psoriasis is a disease which can be correlated with skin diseases (Ekakushta) and the symptoms are absence of perspiration (Asvedana), large area of skin involved (Mahavasthu) and skin resembling the scales of fish (Matsyashakalapam) (Srikantamurthy, 2009g). Inflammatory bowel disease specially refers to disease of bowel with inflammatory changes (Grahaniroga) and the symptoms are expulsion of undigested food (Buktamama eva vimuchyate) with foul smell (Puti) and abdominal pain (Ruja) (Srikantamurthy, 2009h). Multiple sclerosis can be treated as Majjavahasrotovikaras and the symptoms are pain in bones and joints (Bhedoasthiparvanam), loss of muscle (Mamsabalakshaya), loss of sleep (Asvapna) and constant pain in the body (Santataruk) (Srikantamurthy, 2009i).

9. Diagnostic test and interpretation

The laboratory investigation has great value for diagnosing the disease and to understand the disease severity and prognosis of disease of all autoimmune disorders. Components of laboratory investigation including, metabolic panel, inflammatory markers, and auto antibodies which are recently developed and the accuracy is highly beneficial. Antinuclear antibody is most common test to find autoimmune diseases. An antinuclear antibody test is a blood component test that looks for certain kinds of antibodies in the body which is also called fluorescent antinuclear antibody test. It is found in blood of the people suffering from the following disease. Systemic lupus erythematosus, rheumatoid arthritis, scleroderma, sjogren's syndrome. Human leukocyte B27 helps to find the difference between its own cell and foreign substance and it can be positive in up to 8 percent of normal population. C-reactive protein and erythrocyte sedimentation rate are indicators of inflammatory biomarkers in both acute and chronic condition.

10. Conclusion

Autoimmune diseases makes the people prone to easy disabled. Many people can live with an autoimmune diseases, though it is life threatening. Some of the signs and symptoms of autoimmune disorders may change with treatment, food, activities and season. The chances of occurrence of autoimmune disorders in women are much more than men. All the autoimmune diseases are not treatable with modern medication and also the exact etiological factors are unknown. Hence, it is challenging to rule out the causes of all autoimmune diseases, in retrospective methods. Over the past few decades, the food and activities play a major role in the genesis of the disease. Ayurveda is a science which deals with certain diseases which are similar to autoimmune diseases. This science of life helps to manage the condition in a better way by findings out the etiology of diseases in various aspects, such as food habits, life style and other psychological reasons. This review highlight the potential of Ayurveda in addressing the autoimmune disorders through Ayurveda will be shed light for further research in this field.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

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