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Review article

A Review on Autoimmune Diseases: Recent Advances and Future Perspectives

Balid Albarbar[1]*, Hanan Aga[2]

[1]*Department of Medical Laboratory, Higher Institute of Sciences & Medical Technology, Alkums, Libya*
[2]*Department of Nursing, Higher Institute of Sciences & Medical Technology, Alkums, Libya*

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Corresponding Email. *B.albarbar@yahoo.co.uk*

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ABSTRACT

Autoimmune diseases represent a diverse group of disorders characterized by immune-mediated attacks on the body's own tissues and organs. This review provides a comprehensive overview of autoimmune diseases, covering their definition, classification, epidemiology, etiology, pathogenesis, clinical manifestations, current treatments, and future research directions. Autoimmune diseases can be categorized into organ-specific (e.g., type 1 diabetes, Hashimoto's thyroiditis) and systemic (e.g., systemic lupus erythematosus, rheumatoid arthritis) conditions, each with distinct clinical presentations and underlying mechanisms. Genetic predisposition, environmental triggers, and immunological dysregulation play critical roles in disease development. Common symptoms include fatigue, joint pain, skin manifestations, and organ-specific dysfunction, contributing to significant morbidity and impaired quality of life. Current treatment strategies encompass immunosuppressive therapies, disease-modifying drugs, and emerging biologic agents targeting specific immune pathways. Advances in genomics, immunology, and precision medicine offer promising avenues for personalized diagnosis and treatment optimization. Future research directions include further elucidating disease heterogeneity, identifying novel biomarkers, and developing targeted immunotherapies to achieve long-term remission and improve patient outcomes. Understanding the complex interplay of genetic, environmental, and immunological factors is crucial for advancing therapeutic approaches and mitigating the global burden of autoimmune diseases. Enhanced collaboration across disciplines and continued investment in research are essential to translate these insights into clinical practice and benefit patients worldwide.

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INTRODUCTION

The study of autoimmune diseases has evolved significantly over the past century. The concept of autoimmune diseases began to take shape in the late 19th and early 20th centuries with observations of diseases like rheumatoid arthritis and systemic lupus erythematosus (SLE), where the immune system was suspected to be attacking the body's own tissues. In the mid-20th century, landmark discoveries such as the identification of antinuclear antibodies (ANAs) in lupus patients provided critical insights into the autoimmune nature of certain diseases. This period also saw the development of diagnostic tests to detect these antibodies [1,2]. The latter half of the 20th century witnessed rapid advances in

immunology, including the understanding of T-cell and B-cell functions, which shed light on the mechanisms underlying autoimmune responses [3,4]. The discovery and development of immunosuppressive medications, such as corticosteroids and later biologic therapies, revolutionized the treatment of autoimmune diseases, offering new avenues for managing symptoms and slowing disease progression [5]. Today, ongoing research continues to uncover new genetic, environmental, and immunological factors contributing to autoimmune diseases. Advances in genomics, proteomics, and immunotherapy hold promise for personalized treatments and improved outcomes for patients.

Definition of autoimmune disease

Autoimmune diseases are a broad category of disorders characterized by an abnormal immune response against the body's own tissues. In a healthy immune system, specialized cells and proteins (such as antibodies) protect the body against harmful invaders like bacteria and viruses. However, in autoimmune diseases, this defense mechanism malfunctions, leading the immune system to mistakenly attack normal cells and tissues as if they were foreign invaders [6]. Autoimmune diseases can affect virtually any part of the body, including joints (e.g., rheumatoid arthritis), skin (e.g., psoriasis), organs (e.g., type 1 diabetes affecting the pancreas), and the nervous system (e.g., multiple sclerosis). They can vary widely in their severity and impact on health, ranging from mild to debilitating and life-threatening conditions [7].

Prevalence and impact

Autoimmune diseases collectively affect a significant portion of the global population, affecting individuals of all ages and ethnicities. While specific prevalence rates vary by disease type and geographic region, autoimmune diseases are generally recognized as prevalent and increasing in incidence [8,9].

Prevalence trends

The prevalence of autoimmune diseases varies widely, with some estimates suggesting that these conditions collectively affect around 5-8% of the population in developed countries. The incidence and prevalence of specific autoimmune diseases can fluctuate over time and may be influenced by genetic predisposition, environmental factors, and changes in diagnostic criteria and awareness [10,11].

Gender and age distribution

Autoimmune diseases disproportionately affect women more than men, with many conditions showing a female-to-male ratio of 3:1 or higher. Certain diseases, such as SLE and Hashimoto's thyroiditis, often present during reproductive years. However, autoimmune diseases can also affect children and the elderly [12,13].

Geographic variations

There are geographic variations in the prevalence of autoimmune diseases, influenced by genetic factors, environmental exposures (such as infectious agents and diet), and healthcare access. For instance, multiple sclerosis (MS) is more prevalent in temperate regions compared to tropical areas [12,14,15]. Overall, the global epidemiology of autoimmune diseases underscores their significant impact on individuals, healthcare systems, and society as a whole. Addressing these challenges requires collaborative efforts across research, healthcare delivery, public health initiatives, and advocacy to improve outcomes, reduce healthcare disparities, and enhance the quality of life for individuals living with autoimmune diseases.

Clinical manifestations

Autoimmune diseases can present with a wide range of symptoms and signs, depending on the specific disease and organs affected [7]. Some common manifestations for autoimmune disease are shown in table 1.

Table 1. Clinical manifestations of autoimmune diseases

Symptoms	Description
Fatigue	A symptom for many autoimmune diseases
Joint pain and swelling	Arthralgia and arthritis
Skin manifestations	Such as rashes, ulcers and photosensitivity
Fever	Occur in systemic autoimmune diseases
Muscle weakness	Such as dermatomyositis and polymyositis
Neurological symptoms	Such as cognitive impairment and neuropathies
Gastrointestinal issues	Abdominal pain, diarrhea, and malabsorption
Endocrine dysfunction	Leading to symptoms like weight changes

Pathogenesis

Genetic factors

Genetic predisposition plays a significant role in the development of autoimmune diseases. Many autoimmune disorders exhibit familial clustering, suggesting a strong genetic component. Specific genes associated with autoimmune diseases have been identified through genetic studies, including genome-wide association studies (GWAS), reviewed recently in references [16,17]. The human leukocyte antigen (HLA) genes, particularly within the major histocompatibility complex (MHC) region, are the most extensively studied genetic risk factors for autoimmune diseases. Variations in HLA genes influence the presentation of self-antigens to T-cells, thereby affecting immune tolerance. Apart from HLA genes, numerous non-HLA genes have been implicated in different autoimmune diseases [18,19]. These genes often regulate immune responses, such as cytokine production, T-cell activation, and B-cell function. Most autoimmune diseases are polygenic, meaning they involve multiple genetic factors that interact with each other and with environmental influences to determine disease susceptibility [19].

Epigenetic factors

Epigenetic changes (modifications to DNA that affect gene expression without altering the DNA sequence itself) can also influence susceptibility to autoimmune diseases by regulating how immune cells respond to environmental triggers [20,21].

Environmental factors

While genetic factors set the stage for autoimmune diseases, environmental factors play a crucial role in triggering immune dysregulation. These triggers can include: infections, dietary factors, toxins, stress and microbiome [22]. Infections such viral or bacterial infections are known triggers for many autoimmune diseases. For example, Epstein-Barr virus (EBV) infection has been linked to an increased risk of developing multiple sclerosis [23-25]. In addition to autoimmune triggers certain dietary components, such as gluten in celiac disease or iodine in autoimmune thyroid diseases, can trigger immune responses in susceptible individuals. Environmental pollutants like cigarette smoke, industrial chemicals, and heavy metals may contribute to autoimmune diseases by promoting inflammation and oxidative stress [26,27]. Psychological stress has been implicated in exacerbating autoimmune diseases through its effects on immune function and inflammation. Also, alterations in the gut microbiota composition have been associated with autoimmune diseases, suggesting a role for the microbiome in modulating immune responses [22, 28].

Hormonal influences

Studies showed that hormones, particularly sex hormones like estrogen and testosterone [29], can modulate immune responses and affect the prevalence and severity of autoimmune diseases, which often show a gender bias [13,30,31].

Immunological factors

Autoimmune diseases arise from a breakdown of immune tolerance, where the immune system fails to distinguish between self and nonself-antigens, leading to the production of autoantibodies and immune-mediated tissue damage [32]. Key immunological mechanisms involved include: loss of tolerance: mechanisms normally exist to prevent immune cells from attacking self-antigens and failure of central (thymic) and peripheral tolerance mechanisms allows auto-reactive T-cells and B-cells to escape elimination [4,21,33]. Moreover, studies reported that reduction in T regulatory cells number lead to autoimmune disease, reviewed in reference [34,35]. B-cells produce autoantibodies that target self-antigens, forming immune complexes that contribute to tissue damage through complement activation and inflammation [32,36]. Dysregulated production of pro-inflammatory cytokines such as TNF-alpha, IL-6 and anti-inflammatory cytokines such as IL-10 contributes to chronic inflammation and tissue destruction in autoimmune diseases [37]. Activated T-cells, particularly CD4+ T-helper cells and CD8+ cytotoxic T-cells, play central roles in orchestrating immune responses against self-antigens, further perpetuating tissue damage, reviewed recently in reference [17]. Dendritic cells (DCs) as professional antigen-presenting cells (APCs), play a critical role in initiating and regulating immune responses by presenting self-antigens to T-cells and influencing immune tolerance or activation [38,39]. The specific mechanisms vary among different autoimmune diseases. Some diseases may primarily involve antibodies targeting specific tissues (e.g., SLE), while others may involve cytotoxic T cells (e.g., T1DM) or immune complexes (e.g., RA) [40,41]. Overall, autoimmune diseases result from a complex interplay of genetic, environmental, immunological, and hormonal factors. Understanding these factors is crucial for developing better treatments and interventions for these chronic and often debilitating conditions.

Classification

Autoimmune diseases can be classified based on whether they predominantly affect specific organs or tissues (organ-specific) or involve multiple organ systems (systemic) [2,7]. Organ-specific autoimmune diseases predominantly affect a single organ or tissue as some examples presented in table 2, whereas systemic autoimmune diseases involve multiple organs (as shown in table 3) and can have diverse clinical manifestations.

Table 2. Organ-specific autoimmune diseases

Autoimmune disease	Pathophysiology	References
T1DM	Destruction of pancreatic beta cells	[42]
Hashimoto's Thyroiditis	Inflammation of the thyroid gland	[43]
Autoimmune Hepatitis	Destruction of liver cells	[44]
Celiac Disease	Damage of intestinal villi	[45]

Table 3. Systemic autoimmune diseases

Autoimmune disease	Pathophysiology	References
SLE	Immune complex inflammation affecting multiple organs and tissues	[46]
RA	Inflammation of synovial joints leading to progressive joint destruction.	[47]
Sjögren's Syndrome	Destruction of exocrine glands	[48]
Systemic Sclerosis (Scleroderma)	Thickening and hardening of skin and internal organs	[49]

Understanding these classifications is crucial for accurate diagnosis, management, and treatment of autoimmune diseases, as the treatment approach may vary depending on whether the disease is localized or systemic in nature. Ongoing research continues to explore the underlying mechanisms and develop targeted therapies to improve outcomes for patients with autoimmune diseases.

Diagnosis

Diagnosing autoimmune diseases can be challenging due to their varied presentation and the overlap of symptoms with other conditions. Diagnosis typically involves a combination of clinical evaluation, laboratory tests, and sometimes imaging studies as discussed accordingly:

Clinical evaluation

A thorough medical history and physical examination are crucial in identifying symptoms suggestive of autoimmune diseases and assessing their impact on different organ systems [50].

Laboratory tests

Studies showed that laboratory diagnosis involves testing for specific autoantibodies such as investigating anti-nuclear antibodies in SLE, and anti-thyroperoxidase antibodies (anti-TPO antibodies) in Hashimoto's thyroiditis can help confirm the presence of autoimmune processes [51,52]. In addition, measurement of markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) can indicate the presence and severity of inflammation and abnormalities such as anemia or leukopenia may be present in autoimmune diseases. Also, organ-specific tests are used and this is depending on the suspected disease, specific tests may be conducted, such as thyroid function tests in thyroid autoimmune diseases or liver function tests in autoimmune hepatitis [36,53,54].

Additional diagnostic techniques

Imaging tests useful for evaluating joint damage in diseases such as RA. Thus, ultrasound can be used to assess joint inflammation and synovitis [55,56]. Additionally, computed tomography (CT) scan and magnetic resonance image (MRI) provide detailed images of internal organs and tissues, helpful in diagnosing conditions like systemic sclerosis affecting the lungs or kidneys [57]. On the other hand, in some cases, a tissue biopsy such as autoimmune pancreatitis may be necessary to confirm the diagnosis and assess the extent of tissue damage [58].

Challenges in diagnosis

Many autoimmune diseases present with non-specific symptoms that can mimic other conditions, leading to delay in diagnosis. Some patients may exhibit features of multiple autoimmune diseases simultaneously, complicating the diagnostic process. Symptoms can vary widely between individuals and may change over time, making diagnosis challenging, reviewed in references [59,60]. Overall, diagnosing autoimmune diseases requires a comprehensive approach that considers clinical symptoms, laboratory tests for autoantibodies and inflammation markers, and imaging studies when necessary. Early diagnosis is crucial for initiating appropriate treatment and minimizing disease progression and complications in patients with autoimmune diseases. Continued research into diagnostic biomarkers and imaging techniques aims to improve accuracy and efficiency in diagnosing these complex and heterogeneous conditions.

Management of autoimmune diseases

Management of autoimmune diseases can be measured using a variety of approaches aimed at suppressing the abnormal immune response, modifying disease progression, and alleviating symptoms. An overview of current therapeutic strategies are discussed in next sections.

Immunosuppressive therapies

Immunosuppressive therapies are designed to dampen the immune response responsible for attacking the body's own tissues. These treatments are often used to induce remission or control disease activity in autoimmune disorders [61]. For example, prednisone and other corticosteroids are potent anti-inflammatory drugs that suppress immune responses [62]. They are commonly used in acute exacerbations or flare-ups of autoimmune diseases to quickly reduce inflammation and symptoms. In addition to autoimmune therapy, biologic drugs are also used that interfere with specific components of the immune system involved in autoimmune diseases. These drugs include inhibitors such as TNF-alpha inhibitors (such as infliximab, adalimumab, etanercept) are used in diseases such RA and inflammatory bowel disease (IBD) [63,64]. Moreover, IL-6 inhibitors such as tocilizumab targets IL-6 is used in diseases such as RA and systemic juvenile idiopathic arthritis [65,66]. In contrast to inhibitors, monoclonal antibodies are used such as (rituximab) targets $CD20^{+}$ B-cells and is used in diseases such as RA and SLE [67,68].

Disease-modifying therapies

Disease-modifying therapies aim to alter the course of autoimmune diseases by targeting underlying disease mechanisms rather than simply managing symptoms [69]. A disease-modifying anti-rheumatic drug (DMARD): these drugs inhibit or modulate the immune system to slow disease progression and these include the following: Methotrexate is a cornerstone DMARD in RA [70]. Also, hydroxychloroquine is used in SLE and RA to reduce disease activity [71]. In addition, other drugs are used as inhibitors for Janus Kinase (JAK) such as tofacitinib and baricitinib that target the JAK-STAT signaling pathway involved in immune responses. They are used in RA and other inflammatory conditions [72,73].

Emerging therapies

Ongoing research continues to explore novel therapeutic approaches aimed at improving treatment efficacy and reducing side effects. These emerging immunotherapies targeting B and T cells and stem cell therapies as discussed accordingly: newer agents targeting B-cells more specifically than traditional therapies such as anti-CD20 agents like ofatumumab [74]. In contrast to B cells, there are therapies aimed at modulating T-cell responses through novel mechanisms as reported recently in the following references [75,76]. There are also other drugs were used targeting the complement system, implicated in diseases like lupus nephritis [77]. Another therapy were used known as stem cell therapies or hematopoietic stem cell transplantation (HSCT), this therapy aims to reset the immune system in severe cases of autoimmune diseases resistant to conventional therapies [78]. Moreover, mesenchymal stem cells (MSCs) are also employed as therapy due to for their immunomodulatory properties and potential to reduce inflammation in autoimmune diseases [79]. Experimental studies reported that gene therapy approaches to modify immune responses at the genetic level, potentially offering long-term disease control [80]. Overall, while significant progress has been made in treating autoimmune diseases, challenges remain, including managing treatment side effects, ensuring accessibility to newer therapies, and addressing disease heterogeneity among patients. Future research aims to further personalize treatments, improve understanding of disease mechanisms, and develop safer and more effective therapies for autoimmune diseases. Clinical trials exploring novel targets and combinations of therapies are critical in advancing the field and offering hope to patients with challenging autoimmune conditions.

CONCLUSION

In this review of autoimmune diseases, several key points have emerged: autoimmune diseases involve the immune system mistakenly attacking the body's own tissues, categorized into organ-specific (e.g., T1DM) and systemic (e.g., SLE) conditions. Autoimmune diseases pose a substantial global burden, affecting millions worldwide and imposing economic and social challenges on healthcare systems and patients. Genetic predisposition, environmental triggers (such as infections and toxins), and immunological mechanisms (loss of tolerance, autoantibody production) contribute to the development and progression of autoimmune diseases. Increased awareness and recognition of autoimmune disease symptoms can lead to earlier diagnosis and intervention, potentially improving outcomes and reducing long-term complications. Symptoms vary widely but commonly include fatigue, joint pain, skin changes, and organ-specific dysfunction, impacting quality of life significantly. Management strategies include immunosuppressive therapies (corticosteroids, biologics), DMARDs, and emerging therapies targeting specific immune pathways and cells. Genomics, immunological advances, and precision medicine offer promising avenues for personalized diagnosis, treatment optimization, and new therapeutic discoveries. By advancing these areas of research, clinicians and researchers can continue to improve diagnostic accuracy, refine treatment strategies, and ultimately enhance the quality of life for individuals living with autoimmune diseases worldwide. Continued collaboration across disciplines and investment in innovative technologies will be essential in driving these advancements forward.

Conflicts of Interest

The authors declare no conflicts of interest.

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مراجعة الأمراض المناعية الذاتية: التطورات الحديثة والآفاق المستقبلية

بلعيد البربار[1]، حنان آغا[2]

[1]قسم المختبرات الطبية، المعهد العالي للعلوم والتقنيات الطبية، الخمس، ليبيا
[2]قسم التمريض، المعهد العالي للعلوم والتقنيات الطبية، الخمس، ليبيا

المستخلص

الأمراض المناعة الذاتية هي مجموعة من الاضطرابات ناتجة عن هجمات مناعية على أنسجة الجسم وأعضائه. تقدم هذه الدراسة نظرة شاملة لأمراض المناعة الذاتية، تعريفها وتصنيفها وانتشارها ومسبباتها والعلامات السريرية والعلاجات واتجاهات البحث المستقبلي. يمكن تصنيف أمراض المناعة الذاتية الى أمراض خاصة بالأعضاء (مثل مرض السكري من النوع الأول والتهاب الغدة الدرقية هاشيموتو) وأمراض تصيب الأجهزة (مثل الذئبة الحمامية الجهازية والتهاب المفاصل الروماتويدي) ولكل من هذه الأمراض علامات سريرية متميزة وأليات مختلفة. يلعب العامل الوراثي والمحفزات البيئية وخلل التنظيم المناعي أدوارا حاسمة في تطور المرض. تشمل الأعراض الشائعة للمرض التعب، الام المفاصل، أعراض جلدية، والخلل الوظيفي في أعضاء محددة مما يساهم في حدوث المرض وخلل في الحياة. تشمل استراتيجيات العلاج المثبطات المناعية، والأدوية المعدلة للمرض، والعوامل البيولوجية الناشئة التي تستهدف مسارات مناعية محددة. يوفر التقدم في علم الجينات والمناعة والطب الدقيق طرقا واعدة للتشخيص الشخصي وتحسين العلاج. تشمل الاتجاهات البحثية المستقبلية مزيدا من توضيح عدم تجانس المرض، وتحديد المؤشرات الحيوية الجديدة، وتطوير علاجات مناعية مستهدفة لتحقيق وتطوير النتائج. فهم التفاعل المعقد بين العوامل الوراثية والبيئية والمناعية أمر بالغ الأهمية لتعزيز الأساليب العلاجية وتخفيف العبء العالمي لأمراض المناعة الذاتية. يعد التعاون المعزز عبر التخصصات والاستثمار المستمر في الأبحاث أمرا ضروريا لترجمة هذه الأفكار الى ممارسة سريرية ومساعدة المرضى في جميع أنحاء العالم.

الكلمات المفتاحية: أمراض المناعية الذاتية، الجهاز المناعي، الأجسام المضادة.