IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A REVIEW ARTICLE ON AUTOIMMUNE DISEASE: CAUSES AND EVOLUTIONARY PERSPECTIVES

Nameera Khatoon[1] ,Santosh Kumar[2] ,Summa Parween[3], Shyam Mahto[4] and Ravi Ranajn[5*]

[1] Aspiring Researcher, Department of Zoology

R.S. More College, Govindpur, Dhanbad, Jharkhand, India

[2]Associate Professor, Department of Pharmaceutics

Shakuni Choudhary College of Health and Sciences, Munger, Bihar, India

[3]Aspiring Researcher, Department of Zoology

R.S. More College, Govindpur, Dhanbad, Jharkhand, India

[4]Research Fellow, Department of Chemical Science

Bose Institute, Kolkata

[5]Assistant Professor, Department of Zoology

R.S. More College, Govindpur, Dhanbad, Jharkhand, India

***Abstract*-**Autoimmune diseases arise when the immune system mistakenly attacks the body's own cells, leading to chronic inflammation and tissue damage. These disorders, including rheumatoid arthritis, lupus, multiple sclerosis, and type 1 diabetes, are driven by a complex interplay of genetic, environmental, and immunological factors. Genetic predisposition, epigenetic modifications, and environmental triggers such as infections, diet, and microbiome alterations contribute to immune dysregulation. Additionally, molecular mimicry, bystander activation, and the breakdown of immune tolerance further exacerbate autoimmune responses. From an evolutionary perspective, autoimmunity is paradoxical: while immune hyperactivity provides protection against infections, it also increases susceptibility to self-reactivity. The "hygiene hypothesis" suggests that reduced pathogen exposure in modern societies has led to an increase in autoimmune disorders. Similarly, antagonistic pleiotropy proposes that genes conferring enhanced immune responses against infections in early human history may now predispose individuals to autoimmunity. Furthermore, sexual dimorphism plays a crucial role, with females exhibiting a higher prevalence of autoimmune diseases, likely due to hormonal influences and X-chromosome-linked immune regulation.

This review explores the multifactorial origins of autoimmunity while integrating evolutionary theories that explain its persistence in human populations. Understanding these mechanisms can guide novel therapeutic strategies, including precision medicine and immune modulation, to better manage autoimmune diseases. Future research should focus on unraveling gene-environment interactions and evolutionary trade-offs to provide deeper insights into autoimmune pathophysiology and treatment approaches.

Index Terms: **Autoimmune disease, immune dysregulation, genetics, evolution, hygiene hypothesis, antagonistic pleiotropy, immune tolerance**

I. INTRODUCTION

Autoimmunity was first studied by German immunologist Paul Ehrlich in the 20th century, who termed it *horror autotoxicus* [6]. An autoimmune response occurs when the immune system fails to recognize self-antigens, leading to

the destruction of the body's own cells. In 1965, Macfarlane Burnett introduced key immunological concepts, including autoimmune regulation, lymphoid cell maturation, thymic instruction, apoptosis, and the elimination of self-reactive cells [13]. Autoimmune diseases are generally rare yet chronic, with scientists having identified approximately 80 to 100 such conditions [9]. The exact causes of autoimmune diseases remain unclear, though they are known to involve autoantibody production against self-antigens. Studies suggest that genetic predisposition, environmental influences, lifestyle factors, and hormonal imbalances contribute to their development. Notably, individuals diagnosed with one autoimmune disease are at an increased risk of developing others due to immune system dysfunction [8]. Identified risk factors include adverse drug reactions, smoking, exposure to toxins or infections, and obesity [2]. The clinical presentation of autoimmune diseases varies, ranging from acute organ failure, which can be life-threatening, to chronic illnesses with persistent symptoms [10]. Common symptoms include inflammation, fatigue, weight loss, and abdominal pain, though these differ based on disease type and individual factors [14]. Autoimmune diseases, though relatively uncommon, significantly impact morbidity and mortality. Their prevalence, estimated at 3–5% of the population, is influenced by gender, environmental conditions, and geographic location. Women are more susceptible, except in Crohn's disease, where the male-to-female ratio is approximately 1:1.2[1]. Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder that affects multiple organ systems. It arises due to a combination of genetic, epigenetic, environmental, and ecological factors. The disease primarily triggers the activation of both the innate and adaptive immune systems, resulting in autoreactive B cell activation facilitated by T cells. This immune dysregulation leads to the formation and deposition of immune complexes in tissues, initiating an autoimmune response. Depending on the severity, this cascade may be confined to a single organ or extend to widespread systemic involvement [9]. The age of onset also varies, affecting disease prognosis, progression, severity, and long-term complications. An autoimmune disease arises from an abnormal response of the adaptive immune system, wherein it mistakenly identifies healthy cells and functional tissues as foreign invaders and attacks them. The symptoms of autoimmune diseases vary widely, depending on the specific condition and the affected body part. These symptoms are often unpredictable, ranging from mild to severe, and may fluctuate over time. Common manifestations include low-grade fever, fatigue, and general malaise. The precise causes of autoimmune diseases remain uncertain, though they are believed to result from a combination of genetic predisposition and environmental factors. Studies estimate the overall prevalence of autoimmune diseases in the population to be approximately 4.5%, with a gender disparity—2.7% in males and 6.4% in females—partly due to the observation that many individuals develop more than one autoimmune disorder [5].

II.METHODOLOGY

Review Published Literatures

III.RESULT AND OBSERVATIONS

i) Autoimmune diseases arise when the immune system becomes overactive, mistakenly attacking and damaging the body's own tissues.
ii) Under normal conditions, the immune system produces proteins known as antibodies, which help protect against harmful substances like viruses, cancer cells, and toxins.
iii) However, in individuals with autoimmune disorders, the immune system is unable to distinguish between harmful invaders and the body's healthy cells [7].
iv) More than 100 different autoimmune diseases have been identified by doctors, collectively affecting over 24 million people in the United States.
v) The exact causes or triggers of these conditions remain unclear, and treatment primarily aims to suppress immune system activity [7].
vi) Biological Factors Contributing to Autoimmunity
Several biological factors are known to play a significant role in the development of autoimmune disorders. These include sequestered antigens, neoantigens, the breakdown of immune tolerance, loss of immunoregulation, cross-reacting antigens, and molecular mimicry [1]. Sequestered antigens are components of the body that remain hidden from the immune system during its development. However, injuries to organs can expose these antigens, triggering an immune response. Examples include myelin basic protein (associated with multiple sclerosis), sperm antigens post-vasectomy, lens proteins following eye trauma, and heart muscle antigens after a myocardial infarction [4]. Neoantigens are newly formed antigens that result from genetic mutations or modifications caused by physical, chemical, or microbial agents. While they do not directly cause autoimmune diseases, they can influence disease progression. For instance, in rheumatoid arthritis, the presence of citrullinated neoantigens contributes to the formation of autoantibodies [3]. Rheumatic fever develops when a person is infected with Group A Streptococcus bacterium, which shares structural similarities with heart muscle tissues. The immune system produces antibodies against the bacteria, but these antibodies also attack heart tissues, resulting in the disease. Another example is post-streptococcal glomerulonephritis, where streptococcal antigens share epitopes with kidney glomerular structures. Hashimoto's encephalopathy has also been linked to autoantibodies that target both human and sheep brain antigens [10].

IV.DISCUSSION

Autoimmune diseases occur when the immune system mistakenly targets and attacks the body's own tissues, posing a significant and growing challenge in modern medicine. Disorders such as rheumatoid arthritis, lupus, and multiple sclerosis affect millions of people worldwide, leading to a variety of symptoms and long-term health complications.

Evolutionary biology provides valuable insights into the origins and mechanisms of autoimmune diseases, helping to explain why these conditions develop and how they can be better managed [12]. From an evolutionary perspective, understanding these dysfunctions requires examining the immune system's development over time and the trade-offs that may have contributed to such conditions. Throughout evolution, the immune system has been shaped to mount strong responses against infectious diseases. However, this heightened immune activity can sometimes lead to mistakes, such as attacking self-antigens, ultimately resulting in autoimmune disorders. Some theories propose that autoimmune diseases may be an unintended consequence of evolutionary adaptations [15]. For instance, strong immune responses were advantageous in ancestral environments where exposure to infections was common. However, in modern times, improved sanitation and medical advancements have significantly reduced exposure to pathogens. As a result, the same immune mechanisms that once protected humans may now contribute to the development of autoimmune diseases. This trade-off highlights how evolutionary pressures have influenced immune system function, potentially increasing susceptibility to autoimmune disorders in contemporary settings. Genetics play a crucial role in autoimmune diseases, with several key findings emerging from evolutionary research. Numerous genetic variants associated with autoimmune disorders have been identified, many of which are linked to immune system regulation and self-tolerance. Evolutionary biology underscores the significance of genetic diversity within populations [12]. Autoimmune diseases can manifest at different ages and vary across genders, ethnicities, and demographics. Women, in particular, are more prone to these conditions. During the literature review on autoimmune diseases, several remarkable findings emerged. This section explores hypothesis-driven studies related to autoimmune diseases, offering intriguing insights and shedding light on the complex nature of these conditions.

Table 2. Categories of autoimmune diseases

Category (disorders)	**Diseases**
Neurological autoimmune disorders	Encephalitis, optic neuropathies, myelitis, multiple sclerosis, cranial neuropathies
Autoimmune blood disorder	Idiopathic thrombocytopenic purpura, autoimmune haemolytic anaemia
Autoimmune ocular disorder	Retinal vein vasculitis occlusion
Renal autoimmune disorder	Crescentic glomeruli-nephritis good pasture syndrome

V.CONCLUSION

Understanding autoimmune diseases requires knowledge of the biological significance of evolution. The establishment of a specialized defense system against microorganisms has inherently made living organisms susceptible to developing autoimmune conditions. The presence of various regulatory mechanisms can be understood as evolutionary strategies designed to prevent self-destruction.

Humans, having undergone cumulative evolutionary changes, possess highly complex innate and adaptive immune systems, which in turn increase their susceptibility to autoimmunity. Research on autoimmunity and immune responses continues to expand, necessitating further studies to uncover underlying mechanisms and unanswered questions.

Advancements in diagnostic methods, such as multiplex technology, are improving detection, and with the rapid development of AI technology, it is expected that within the next decade, we may be able to predict an individual's risk of developing autoimmune diseases. While some treatments for autoimmune disorders are currently in use, others remain under clinical trials, aiming to enhance therapeutic options.

VI.CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

REFERENCES

1. Angum F, Khan T, Kaler J, Siddiqui Hussain A; 2020, 12: e 8094: The prevalence of autoimmune Disorders in human.
2. CC Medical Professional; 2021: Autoimmune Diseases: Causes, Symptoms, IT and Treatment Cleaveland Clinic
3. Guo Q, Gatto M, Domeneghetti M, Palma L, Borella E, Iaccarino L, et al. ;2013; Clinical guidelines and definitions of auto inflammatory diseases: contrasts and comparisons with autoimmunity-a comprehensive review; Clinical Reviews in Allergy & Immunology;**45 (2);**227-235.
4. Harakal J, Qiao H, Wheeler K, Rival C.;2022; Exposed and sequestered antigens in testes and their protection by regulatory T cell-dependent systemic tolerance; Front Immunol
5. Hayter S.M., Cook M.C.;2012; Updated assessment of the prevalence, spectrum and case definition of autoimmune disease; Autoimmunity Reviews**;(10);**754-765
6. Koppla SN and Guruprasad V;2023; Overview of autoimmunity: Classification, diseases and Etiology; Turk. J Immunol;**11(3)**: 93 - 105.
7. Kris M, Zilpah S, MD; 2023; Web MD.
8. Limr, F; 2023: Autoimmune diseases: Types, Risk factors, Diagnosis and More, “Medical News Today
9. Muhammad Atif Ameer, Chaudhry, Mushtaq, Osama , Maham Babar , Tehmina Hashim , Saima Zeb , Muhammad Ali Tariq , Sridhar Reddy Patlolla , Junaid Ali , Syeda Nafeesa Hashim , Sana Hashim;2022;An Overview of Systemic Lupus Erythematosus (SLE) Pathogenesis, Classification, and Management;**14(10)**;e30330;doi: 10.7759/cureus.30330
10. Orabai Marie A; 2018; What you have to know about Autoimmune diseases.
11. Pisetsky D.S., Nat Rev Nephrol; 2023: Pathogenesis of autoimmune disease; Nat Rev Nephrol; **19;**509-24.
12. Robert MH, Edrei E; 2020, 19: 102423: Comparative United State autoimmune disease rate by sex.
13. Vanderbilt University USA;2024; Department of Paediatrics
14. Wang L and Wang F.S.; 2015; Human autoimmune diseases; Human autoimmune disease: a comprehensive update Intern Med.; 278:369-95.
15. Watson S. Healthline Media; 2017: Autoimmune Diseases: types, symptoms causes and more.
16. Xing Y and Hogquist K.A.; 2012; T - Cell Tolerance: Central and Peripheral;**4**;a 006957