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Autoimmune Diseases: A Serious Medical, Economic and Social Issue

Hassan AU[1], Ugochukwu OO[1], Onuh K[1], Kereakede E[1] and Umar SI[2]

[1]Department of Biotechnology, Nigerian Defence Academy, Kaduna, Nigeria.
[2]Department of Microbiology, Bayero University Kano, Nigeria

Corresponding Author's Email: abbahu@nda.edu.ng

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Abstract

Autoimmune diseases are currently registering an alarming incidents worldwide since the end of the Second World War. Usually as the consequence of a breach in immune tolerance, leading to the inability to sufficiently differentiate between self and non-self. Immune reactions that are usually targeted towards self-antigens can however lead to the destruction of the host's cells and the development of autoimmune diseases. Although autoimmune disorders are comparatively rare, the worldwide incidence and prevalence is increasing and they have major adverse implications for mortality and morbidity. Genetic and environmental factors are thought to be the major factors contributing to the development of autoimmunity. However, viral infections are also one of the environmental triggers that can lead to autoimmunity. Current research suggests that several mechanisms, such as molecular mimicry and bystander activation, can cause viral-induced autoimmunity. Here, we overviewed the latest insights into the mechanisms of autoimmunity, Immunological Tolerance, classes, causes and epidemiology of autoimmune diseases, with some insight in some of Nigerian most skyrocketing autoimmune diseases.

Keywords: Autoimmunity, Immunology, Genetic, epidemiology, Cells, Diseases

1.0 INTRODUCTION

Autoimmune disease is the clinical manifestation of abnormalities in immune regulation that leads to tissue damage by self-reactive lymphocytes and autoantibodies, resulting in debilitating symptoms and death when vital organs are affected (Huffake *et al*., 2021). The causes of most autoimmune

diseases remain uncertain, although environmental factors are strongly indicated through studies in animal models. Autoimmune diseases are often treated with steroids. (Patt *et al*., 2013). These kinds of diseases have registered an alarming increase worldwide since the end of the Second World War. This pandemic includes more than 80 autoimmune disorders and increases in both the incidence and prevalence of autoimmune disorders such as Crohn's disease, rheumatoid arthritis, multiple sclerosis and type I diabetes (Sutherland *et al*., 2009). All these includes a variety of diseases which can be described by the irregular functioning of the immune system that causes an individual's immune system to generate antibodies which attack their own body tissues. The development of autoimmune

disease occurs as a result of an overactive immune response to body material and tissues present in the body (Jog *et al*., 2020). This means that the body attacks its own cells. The immune system confuses a specific part of the body as a pathogen and attacks it. This could be restricted to specific organs (e.g. autoimmune thyroiditis) or it could involve a specific tissue in various places (e.g. Good pasture's disease which may have an effect on the basement membrane in both the lungs and kidneys). Immunosuppression, which is a disease medication that decreases the immune response, is typically the treatment of an autoimmune disease. An individual's immune system protects one from disease and infection, however, If a person has an autoimmune disease, their immune system inaccurately attacks healthy cells in their body. These diseases tend be genetic (Lo *et al*., 2021). Women, in particular, African-American, Hispanic-American, and Native-American women - have a higher risk for certain autoimmune disorders. There are currently more than eighty various kinds of autoimmune diseases, and many of them have alike symptoms. This makes it difficult for a person's general practitioner to know if they really have one of these diseases, and if so, which one. Obtaining a diagnosis may be frustrating and stressful. In many people, the first symptoms are being fatigued, having muscle aches and developing a low grade fever. These diseases may also have cycles of flare-ups, when they get worse, and remissions, when they recede (Galea *et al*., 2021). The diseases do not usually go away however, symptoms can be treated. In certain cases, the antibodies may not be directed at a specific tissue or organ; for example, antiphospholipid antibodies can react with substances such as phopholipids that are the normal components of blood platelets and the outermost layer of cells (cell membranes), which can lead to the formation of blood clots within the blood vessels as in thrombosis. Immune tolerance is defined as specific non-reactivity of the immune system to a particular antigen, which is capable under other circumstances of inducing an immune response (Marchetti *et al*., 2020). The administration of antigens either at high or low dose and infection with certain viruses during critical early stages of immunological development may also aid in inducing tolerance. According to the American Heritage Medical Dictionary, central tolerance occurs during lymphocyte development and functions in the thymus and bone marrow. Here, T and B lymphocytes that recognize self-antigens are deleted before they develop into fully immunocompetent cells and preventing autoimmunity (Bjornerik *et al*., 2022). This process is most active in foetal life, but continues throughout life as immature lymphocytes are generated. Positive selection occurs first when naive T-cells are exposed to antigens in the thymus. T-cells which have receptors with sufficient affinity for self-MHC molecules are selected. Other cells that do not show sufficient affinity to self-antigens will undergo a deletion process known as death by neglect which involves apoptosis of the cells. The positive selection is a classic example of the importance of some degree of auto-reactiveness. This does not occur in B-cells (Bjornerik *et al*., 2023). This study is aimed at overviewing **Autoimmune Diseases,** as a serious medical, economic and social issue in Nigeria and the world as a whole.

2.0 LITERATURE FINDINGS

2.1 MECHANISM OF AUTOIMMUNITY

One definition of the immune system is that it is an intricate set of cellular, chemical and soluble protein mechanisms, intended to shield the body against alien substances such as infections and tumour cells, without attacking self-molecules (Mouat *et al*., 2022). Antigens are those molecules (self or alien molecules) which evoke specific immune responses in the body. Immune cells are situated throughout the entire body. Organs such as the spleen, thymus, skin and gut contain immune cells tactically placed in order to screen the entry of alien substances. Optimum functioning of the immune system occurs when the immune cells and cell products work together with each other in a sequential and harmonious manner (Autin *et al*., 2019). The immune system specifically recognizes and eliminates foreign agents thereby protecting the host against infection. During maturation of the immune system, immune cells that react against self-tissues are eliminated providing an immune system that is 'tolerant' to self. Historically, autoimmunity or reactivity of the immune system to self-antigens was thought of as an aberrant response. More recently, researchers have realized that autoimmunity is a natural phenomenon, with

self-reactive antibodies and autoimmune cells present in all normal individuals (Marchetti *et al*., 2020). Antiself responses are usually generated in the process of mounting an immune response to foreign antigens, but autoimmune disease results only if autoimmunity is poorly regulated. A combination of genetic predisposition and environmental factors contribute to the development ofautoimmune disease (Ball *et al*., 2015). The distinction between self-molecules and alien substances occurs through intricate mechanisms that are dependent on certain recognition molecules present on the surface of immune competent cells, specifically, T and B lymphocytes. There are non-specific effector mechanisms which complement the T and B lymphocytes to serve as the first line of defence against possible pathogens. These cells can be leukocytes such as macrophages, natural killer cells and polymorphonuclear leukocytes. There are also soluble mediators such as cytokines which play a role in the body's defence structure (Waldman *et al*., 2020). A small percentage of T and B lymphocytes form a normal part of the immune cell pool. Tolerance is preserved by the controlled interactions of various cell types and soluble mediators. However, in certain environments, tolerance can be broken and this results in an autoimmune pathogen. The development of autoimmune diseases are highly dependent on genetics, yet other factors such as viruses, bacterium or chemical exposure play as contributors to changes in self-reactivity (Huang *et al*., 2019). There are various symptoms and disorders which are encompassed in autoimmune diseases. They vary from organ specific to systemic, and include, insulin dependent diabetes mellitus, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, thyroiditis and multiple sclerosis to name but a few. The most common areas in the body which are targeted by autoimmune diseases are the thyroid gland, stomach, adrenal glands and pancreas (Steenblock *et al*., 2021).

2.2 IMMUNOLOGICAL TOLERANCE

Pioneering work by Noel Rose and Ernst Witebsky in New York, and Roitt and Doniach at University College London provided clear evidence that, at least in terms of antibody-producing B lymphocytes, diseases such as rheumatoid arthritis and thyrotoxicosis are associated with loss "non-self". This breakage leads to the immune system's mounting an effective and specific immune response against self determinants (Sherina *et al*., 2017). The exact genesis of immunological tolerance is still elusive, but several theories have been proposed since the mid-twentieth century to explain its origin.

Three hypotheses have gained widespread attention among immunologists:

i. **Clonal Deletion theory**, proposed by Burnet, according to which self-reactive lymphoid cells are destroyed during the development of the immune system in an individual. For their work Frank M. Burnet and Peter B. Medawar were awarded the 1960 Nobel Prize in Physiology or Medicine "for discovery of acquired immunological tolerance".
ii. **Clonal Anergy theory**, proposed by Nossal, in which self-reactive T- or B-cells become inactivated in the normal individual and cannot amplify the immune response
iii. **Idiotype Network theory**, proposed by Jerne, wherein a network of antibodies capable of neutralizing self-reactive antibodies exists naturally within the body (*Jerne, 1974).*

In addition, two other theories are under intense investigation:

i. **Clonal Ignorance theory**, according to which autoreactive T cells that are not represented in the thymus will mature and migrate to the periphery, where they will not encounter the appropriate antigen because it is inaccessible tissues. Consequently, auto-reactive B cells, that escape deletion, cannot find the antigen or the specific helper T-cell (*Jerne, 1974).*
ii. **Suppressor population** or **Regulatory T cell theory**, wherein regulatory T-lymphocytes (commonly $CD4^{+}FoxP3^{+}$ cells, among others) function to prevent, downregulate, or limit autoaggressive immune responses in the immune system (Tahmasebinia *et al*., 2017).

Tolerance can also be differentiated into "Central" and "Peripheral" tolerance, on whether or not the above-stated checking mechanisms operate in the central lymphoid organs (Thymus and Bone Marrow) or the peripheral lymphoid organs (lymph node, spleen, etc., where self-reactive B-cells may be destroyed). It must be emphasised that these theories are not mutually exclusive, and evidence has been mounting suggesting that all of these mechanisms may actively contribute to vertebrate immunological tolerance (Virtanen *et al*., 2012).

2.3 CLASSIFICATION OF AUTOIMMUNE DISEASES

Autoimmune diseases can generally be divided into two:

i. Systemic Autoimmune Diseases:
Systemic disorders involve antibodies that are not specific to antigens found on certain tissues (Quaglia *et al*., 2021). Examples include; Systemic lupus erythematosus, Goodpasture's syndrome, Sarcoidosis, Scleroderma, Rheumatoid arthritis and Dermatomyositis

ii. Localised Autoimmune Diseases: these are specific to a particular tissue or organ. It can be divided into the following groups;
   a. Dermatologic diseases ie Sjogren's syndrome, Scleroderma, Dermatomyositis, Psoriasis, Vitiligo, Alopecia areata (Sundaresan *et al*., 2023)
   b. Endocrinologic diseases ie Type 1 diabetes mellitus, Autoimmune pancreatitis, Hashimoto's thyroiditis, Addison's disease (Tengvall *et al*., 2019), Neurologic diseasesMultiple sclerosis, Myasthenia gravis (Jog *et al*., 2020)
   c. Hermatologic diseases ie Polyarteritis nodosa, Idiopathic thrombocytopenic purpura, Hemolytic anemia, Antiphospholipid antibody syndrome and Pernicious anemia (Lee *et al*., 2020)
   d. Gastrointestinal disease ie Celiac disease, Inflammatory bowel disease, Autoimmune hepatitis and Primary biliary cirrhosis (Sundaresan *et al*., 2023)

2.3.1 CAUSES

It is widely accepted that the pathogenesis of autoimmune diseases is multifactorial, where the genetic, infectious and environmental factors play a role in determining the onset and progression of the disease. Despite this, the ability to quantify the environmental influences of autoimmune diseases is extremely difficult. Various evidences suggest that genetic factors are a major determinant of autoimmune disease susceptibility as well as progression (Marchetti *et al*., 2020).

2.4 RHEUMATOID ARTHRITIS

Rheumatoid arthritis is a chronic inflammatory disease, producing joint damage mediated by cytokines, chemokines, and metalloproteases. It is speculated that rheumatoid arthritis is a relatively new disease because there is a surprising lack of historical evidence for its existence (Gonzalez *et al.*, 2007). The disease is systemic characteristically affecting the synovial joints and periarticular synovial structures (bursae and tendon sheaths) in particular). This typically starts with the small bones of the hands and feet, although any joint can be involved. In advanced cases of the condition, most joints are become affected (Fechtner *et al*., 2022). The systemic nature of the condition means that many other organs may become involved as the condition progresses. Examples of extra-articular involvement can include symptoms and effects such as fever, weight loss, fatigue or weakness, swollen lymph nodes, anemia, nodules, dry eyes, fibrosis of the lungs, fluid in the chest cavity, vasculitis, neuropathy, GI, and kidney disease. The trigger for the disease is not known, but is thought to be autoimmune. The condition is variable in its initial presentation. Symptoms can occur either as a single episode of stiff and painful joints which may last some months, or as an aggressive and destructive condition which progresses rapidly, and if unchecked, leads to severe physical disability (Cancro *et al*., 2020). Characteristically however the disease usually presents as a small joints bilateral polyarthritis. The condition is follows a pattern of remission and relapse over many years. The main joint pathology in rheumatoid arthritis is an auto-immune mediated thickening and inflammation of the synovial membrane, which becomes infiltrated with inflammatory cells (Ricker *et al*., 2021).

2.4.1 EPIDEMIOLOGY

The highest prevalence is found among the Native American populations. Prevalence among Caucasian North American and European populations is of the order of 0.5 to 1 %. Population studies from South Africa, especially the rural black populations, have shown a low prevalence. On the contrary, reports from Zimbabwe showed that prevalence of RA may be as high as among Caucasians and that there is no difference in the frequency between the rural and urban populations . RA, on the other hand, had been reported as rare among West Africans (Adelowo *et al.*, 2013).
However, recent reports from Nigeria in which 200 cases of RA were reported may negate this. RA presently constitutes 10 – 15% of the rheumatologic cases seen in many of the rheumatology clinics in Nigeria. Other reports from Burkina Faso ; Kenya ; Cameroun ; South Africa; Democratic Republic of Congo ; Senegal ; also indicate that this condition may not be rare after all (Adelowo *et al*., 2010).

2.4.3 CAUSES

Although rheumatoid arthritis is regarded as an autoimmune disease, details of its pathogenesis remain unclear. It is probably a multifactorial disease which occurs when several risk factors occur simultaneously (Fechtner *et al.,* 2022). There is considerable evidence for an important genetic component and a substantial portion of this risk seems to lie in the presence of class II allele human leukocyte antigen (HLA-DRw4) Variants of PTPN22 and other genes have also been identified as risk factors for RA. There are a number of non-genetic factors which have been suggested. Predominant non-genetic theories include suggestions than an infective cause or trigger is involved, and that environmental influences may play a part. Several observations suggest that the inflammation in rheumatoid arthritis is a T-Cell mediated phenomenon. Cigarette smoking is also thought to play a role. It has been suggested that the risk of developing rheumatoid arthritis is almost twice as high in smokers than in non-smokers (Quaglia *et al.*, 2021). More recent studies indicate that the risk is especially high in males who are rheumatoid factor positive, and in both male and female heavy smokers. The onset of rheumatoid arthritis has a seasonal variation, onset of the condition occurs almost twice as commonly in the winter than in other seasons. The reason for this is not known (Jenks *et al.,* 2019).

2.4.2 SYMPTOMS

Presentation of rheumatoid arthritis is extremely variable but typically follows a relapsing and remitting course. The condition should be suspected in any patient with persistent synovitis, where no other obvious cause can be found. Onset of the condition can be acute with simultaneous inflammation in multiple joints but is more often insidious with progressive joint involvement (Lee *et al.,* 2020). The small joints of the hands (PIP and MCP) and feet (MTP) are often the first joints to be affected, and progression is usually symmetrical. Wrists, elbows and ankles are also typically involved but any joint may be affected. The condition results in joints becoming tender, swollen and warm with both stiffness and limitation of function; resulting in both active and passive movements becoming limited (Cruz *et al.,* 2017). Affected joints can feel ‘boggy’ and tender on palpation. The stiffness results from joint effusion and florid synovitis and is commonly worse in the morning or after periods of inactivity, but does not usually improve after 30 minutes as with osteoarthritis. Pain is present which is worse at rest or after periods of inactivity. Tenderness of affected joints is a very sensitive sign and synovial thickening, eventually of all affected joints, is a most specific sign (Scully *et al.,* 2020).

Rheumatoid Arthritis is a systemic disease and can present with a number of extra-articular conditions, especially as the condition progresses and disease activity increases. Signs of systemic involvement include fever, anorexia, fatigue, swollen lymph nodes, anaemia, nodules, dry eyes, fibrosis of the lungs, fluid in the chest cavity, vasculitis, neuropathy, GI, and kidney disease. Signs and symptoms of rheumatoid arthritis and presentation of the condition can also be affected by the presence of comorbid conditions (Ball *et al.,* 2015).

After a variable period of time, rheumatoid arthritis may become inactive and may then be described as “burn out". At this stage there may be no swelling or redness, but deformed joints, surgical scars and

muscle wasting may all be evident (Costenbader *et al.*, 2008). Non-Articular Involvement

The degree of non-articular involvement (the systemic features of the disease) varies and may precede articular disease. Non-articular symptoms include:

i. General malaise – which can vary from a feeling of being a bit 'off colour' to marked fatigue
ii. Fever
iii. Sweats
iv. Weight Loss
v. Involvement of other body systems (for example eye, lungs, heart)
vi. Lymphadenopathy (Tahmasebinia *et al*., 2017)

2.4.5 DIAGNOSIS

Early diagnosis is key to the management of rheumatoid arthritis, in order to prevent damage to joints and extra-articular complications, to avoid costly medical treatment and surgical interventions, and to prevent the development of functional limitation (Waldman *et al*., 2020). There are a number of challenges to achieving this early diagnosis. Evidence indicates that one of the main barriers to the early initiation of treatment for rheumatoid arthritis is that an affected individual may not recognise the potential severity of the symptoms and therefore delays seeking a medical opinion (Cruz *et al*., 2017). Public awareness of rheumatoid arthritis as a condition is not high. Although the common symptoms and signs are joint swelling, stiffness and deformity, nodules, vasculitis and malaise, this is often of slow onset with progressive joint involvement which may mean that an individual considers the symptoms to be minor or mistakenly attributes the symptoms to normal signs of the aging process (Costenbader *et al.*, 2008).

2.4.6 LABORATORY INVESTIGATIONS

Other laboratory investigations which may be of value include:

i. Inflammation markers - erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) or plasma viscosity - markers are usually raised in rheumatoid arthritis (but may be normal). It should be noted though, that baseline CRP has been shown to be a poor predictor of whom will develop rheumatoid arthritis.
ii. Full blood count (FBC): Normochromic, normocytic anaemia and reactive thrombocytosis common in active disease (Ji *et al*., 2013).
iii. Urea & electrolytes (U&E) to provide a baseline renal function measurement – most treatments for rheumatoid arthritis can have an adverse effect on renal function
iv. Liver function tests (LFT): Mild elevation of alkaline phosphatase and gamma-GT common in active disease.
v. Uric acid/ synovial fluid analysis will assist in excluding polyarticular gout
vi. Urinalysis Microscopic: haematuria/proteinuria may suggest connective tissue disease
vii. Rheumatoid factor (RF) - It should be noted this is only positive in 60-70% RA patients.
viii. Antinuclear antibody (ANA) Positive in SLE and related conditions, and in up to one third of RF-positive RA patients. This test may show some positivity in approximately 10% of individuals who have no disease present (Brossart *et al*., 2020).

2.4.7 IMAGING

Imaging investigations which may be of value include:

i. Radiological Investigation – this may show periarticular osteopenia and/or erosions. A chest x-ray is often performed to exclude lung involvement.
ii. Ultrasound and magnetic resonance imaging – Evidence suggests that ultrasound and MRI scans are highly

sensitive at detecting synovitis, erosions and early inflammatory and damage signs that would not be detected on conventional x-rays. There is little evidence however, on the long term significance of these findings (Woodruff *et al*., 2020). **Treatment**

Treatment options for rheumatoid arthritis have changed dramatically over the last decade, with a differing approach to the initiation of disease modifying anti-rheumatic drugs and the

development of new and more effective medications meaning that early and aggressive intervention can often achieve disease remission before substantial joint damage and disability have occurred (Fechtner *et al*., 2022).

2.5. TYPE 1 DIABETES MELLITUS

Diabetes mellitus type 1 also known as type 1 diabetes, formerly insulin-dependent diabetes or juvenile diabetes is a form of diabetes mellitus that results from the autoimmune destruction of the insulin-producing beta cells in the pancreas. The subsequent lack of insulin leads to increased blood and urine glucose (Xie *et al*., 2022). The classical symptoms are polyuria (frequent urination), polydipsia (increased thirst), polyphagia (increased hunger) and weight loss. The cause of diabetes mellitus type 1 is still unknown. Administration of insulin is essential for survival. Insulin therapy must be continued indefinitely and typically does not impair normal daily activities. People are usually trained to independently manage their diabetes; however, for some this can be challenging. Untreated, diabetes can cause many complications. Acute complications include diabetic ketoacidosis and nonketotic hyperosmolar coma. Serious long-term complications include heart disease, stroke, kidney failure, foot ulcers and damage to the eyes. Furthermore, complications may arise from low blood sugar caused by excessive insulin treatment (Steenblock *et al*., 2021).

Diabetes mellitus type 1 accounts for between 5% and 10% of all diabetes cases. Globally, the number of people with DM type 1 is unknown, although it is estimated that about 80,000 children develop the disease each year. Within the United States the number of affected persons is estimated at one to three million. The development of new cases vary by country and region; the lowest rates appear to be in Japan and China with approximately 1 person per 100,000 per year; the highest rates are found in Scandinavia where it is closer to 35 new cases per 100,000 per year. The United States and other countries in northern Europe fall somewhere in between with 8-17 new cases per 100,000 per year (Lo *et al*., 2021).

2.5.1 SIGNS AND SYMPTOMS

The classical symptoms of type 1 diabetes include: polyuria (excessive urination), polydipsia (increased thirst), xerostomia (dry mouth), polyphagia (increased hunger), fatigue and weight loss. Many type 1 diabetics are diagnosed when they present with diabetic ketoacidosis. The signs and symptoms of diabetic ketoacidosis include xeroderma (dry skin), rapid deep breathing, drowsiness, abdominal pain, and vomiting (Virtanen *et al.,* 2003).

2.5.2 CAUSE

The cause of type 1 diabetes is unknown. A number of explanatory theories have been put forward, and the cause may be one or more of the following: genetic susceptibility, a diabetogenic trigger, and/or exposure to an antigen (Unanun *et al*., 2014).

2.5.3 GENETICS

Type 1 diabetes is a disease that involves many genes. More than 50 genes are associated to type 1 diabetes. Depending on locus or combination of loci, they can be dominant, recessive, or somewhere in between. The strongest gene, *IDDM1*, is located in the MHC Class II region on chromosome 6, at staining region 6p21. Certain variants of this gene increase the risk for decreased histocompatibility characteristic of type 1 (Gordon *et al*., 2017).

2.5.4 ENVIRONMENTAL

Environmental factors can influence expression of type 1. For identical twins, when one twin has type 1 diabetes, the other twin only has it 30%–50% of the time. Thus for 50%-70% of identical twins where one has the disease, the other will not, despite having exactly the same genome; this suggests environmental factors, in addition to genetic factors, can influence the disease's prevalence (Weck *et al*., 2008). Other indications of environmental influence include the presence of a 10-fold difference in occurrence among Caucasians living in different areas of Europe, and that people tend to acquire the rate of disease of their particular destination country (Knip *et al*., 2005).

2.5.6 VIRUS

One theory proposes that type 1 diabetes is a virus-triggered autoimmune response in which the immune system attacks virus-infected cells along with the beta cells in the pancreas (Steenblock *et al*., 2021). The Coxsackie virus family or rubella is implicated, although the evidence is inconclusive. This vulnerability is not shared by everyone, for not everyone infected by the suspected virus develops type 1 diabetes. This has suggested presence of a genetic vulnerability and there is indeed an observed inherited tendency to develop type 1. It has been traced to particular HLA genotypes, though the connection between them and the triggering of an autoimmune reaction remains poorly understood (Xie *et al*., 2022).

2.5.7 CHEMICALS AND DRUGS

Some chemicals and drugs selectively destroy pancreatic cells. Pyrinuron (Vacor), a rodenticide introduced in the United States in 1976, selectively destroys pancreatic beta cells, resulting in type 1 after ingestion. Pyrinuron was withdrawn from the U.S. market in 1979 but is still used in some countries. Streptozotocin (Zanosar), an antibiotic and antineoplastic agent used in chemotherapy for pancreatic cancer, kills beta cells, resulting in loss of insulin production. Other pancreatic problems, including trauma, pancreatitis, or tumors (either malignant or benign) can also lead to loss of insulin production (Tengvall *et al*., 2019).

Table 1: WHO Diabetes Diagnostic Criteria

Condition Unit	2 hour glucose mmol/l(mg/dl)	Fasting glucose mmol/l(mg/dl)
Normal	<7.8 (<140)	<6.1 (<110)
Impaired fasting glycaemia	<7.8 (<140)	≥6.1(≥110) & <7.0(<126)
Impaired glucose tolerance	≥7.8 (≥140)	<7.0 (<126)
Diabetes mellitus	≥11.1 (≥200)	≥7.0 (≥126)

(*Vijan, S March 2010)*

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following:

i. Fasting plasma glucose level at or above 7.0 mmol/L (126 mg/dL).
ii. Plasma glucose at or above 11.1 mmol/L (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test.
iii. Symptoms of hyperglycemia and casual plasma glucose at or above 11.1 mmol/L (200 mg/dL).
iv. Glycated hemoglobin (hemoglobin A1C) at or above 48 mmol/mol (≥ 6.5 DCCT %). (This criterion was recommended by the American Diabetes Association in 2010, although it has yet to be adopted by the WHO) (Roy and Lloyd, 2012).

About a quarter of people with new type 1 diabetes have developed some degree of diabetic ketoacidosis (a type of metabolic acidosis which is caused by high concentrations of ketone bodies, formed by the breakdown of fatty acids and the deamination of amino acids) by the time the diabetes is recognized (Galea *et al*., 2021).

2.5.8 PREVENTION

Type 1 diabetes is not currently preventable. Some researchers believe it might be prevented at the

latent autoimmune stage, before it starts destroying beta cells (*Bluestone et al., 2010*).

2.5.9 IMMUNOSUPPRESSIVE DRUGS

Cyclosporine A, an immunosuppressive agent, has apparently halted destruction of beta cells (on the basis of reduced insulin usage), but its kidney toxicity and other side effects make it highly inappropriate for long-term use (Sundaresan *et al*., 2023).

2.5.10 DIET

Some research has suggested breastfeeding decreases the risk in later life, however various other nutritional risk factors are being studied, but no firm evidence has been found. Giving children 2000 IU of Vitamin D during their first year of life is associated with reduced risk of type 1 diabetes, though the causal relationship is obscure (Sutherland *et al*., 2009).

2.5.11 MANAGEMENT

I. Lifestyle

As psychological stress may have a negative effect on diabetes, a number of measures have been recommended including: exercising, taking up a new hobby, or joining a charity among others (Catriona *et al*., 2022).

ii. Insulin

There are four main types of insulin, rapid acting insulin, short acting insulin, intermediate acting insulin, and long acting insulin. The rapid acting insulin is used as a bolus dosage. The action onsets in 15 minutes with peak actions in 30 to 90 minutes. Short acting insulin action onsets within 30 minutes with the peak action around 2 to 4 hours. Intermediate acting insulin action onsets within 1 to 2 hours with peak action of 4 to 10 hours. Long acting insulin is usually given once per day. The action onset is roughly 1 to 2 hours with a sustained action of up to 24 hours (Bluestone *et al.,* 2010).

Because of the insulin deficiency, injections of insulin either via subcutaneous injection or insulin pump is necessary for those living with type 1 diabetes. It cannot be treated by diet and exercise alone. In addition to insulin therapy dietary management is important. This includes keeping track of the carbohydrate content of food and careful monitoring of blood glucose levels using glucose meters. Today, the most common insulins are biosynthetic products produced using genetic recombination techniques; formerly, cattle or pig insulins were used and even sometimes insulin from fish (Steenblock *et al*., 2021).

iii. Pancreas transplantation

In some cases, a pancreas transplant can restore proper glucose regulation. However, the surgery and accompanying immunosuppression required may be more dangerous than continued insulin replacement therapy, so is generally only used with or some time after a kidney transplant (Muller *et al*., 2021). One reason for this is that introducing a new kidney requires taking immunosuppressive drugs such as cyclosporine (Jennifer *et al.,* 2011). Nevertheless, this allows the introduction of a new pancreas to a person with diabetes without any additional immunosuppressive therapy. However, pancreas transplants alone may be beneficial in people with extremely labile type 1 diabetes mellitus (Saydah *et al.,* 2011).

3.0 CONCLUSION

Autoimmune disorders objectively cannot be cured, but can however be controlled or manage. Historically, treatments usually include; anti-inflammatory pharmaceutics, corticosteroids, synthetic and therapy management.

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