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Management of Patients with Type1 Diabetes and Autoimmunity in the Emergency Room

Dr. Ahmad Mohammad Issa Al-Masri[1*], Dr. Hazim Abdelwahab Abdalla Titi[2]

[12]Specialist Emergency Medicine, PHCC, Jordan

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***Corresponding author:** Dr. Ahmad Mohammad Issa Al-Masri
Specialist Emergency Medicine, PHCC, Jordan
Email: aalmasri020@gmail.com

Abstract **Review Article**

As an autoimmune disorder, type 1 diabetes (T1D) is a serious health problem. It's becoming more commonplace as time goes on. The primary goal of this literature review is to examine how early on in the course of T1D treatment emergency departments might be involved in the care of patients who develop autoimmune disorders. Patients with type 1 diabetes are frequently admitted to the hospital, and it is important to screen them for other autoimmune disorders as part of any trial of treatment. Given the significance of the link between T1D and the development of autoimmune diseases, emergency physicians should be prepared to screen for these conditions, and the emergency department policy should be revised to include the provision of screening tools like appropriate questionnaires and a panel of representative autoimmune disease tests.

Keywords: Type 1 diabetes, autoimmune diseases, emergency department, questionnaire**,** screening policy.

1. INTRODUCTION

The current study conducted a literature review on previous research regarding autoimmunity and type 1 diabetes (T1D) in patients who sought treatment at an emergency room. The following sections will cover a variety of subjects that are connected to one another.

2. Family History of Autoimmunity and T1D

Kossiva *et al.,* (2022) conducted a study to examine how a family history of autoimmunity affects the age at which type 1 diabetes (T1D) symptoms arise, their severity, and the existence of additional autoimmune disorders. The researchers reviewed the medical records of 121 children and adolescents (63 were male) who visited their diabetic clinic between 2002 and 2016. Results showed that Hashimoto's thyroiditis (49.5% of patients) and type 1 diabetes (22.3%). 62.8% of patients had an autoimmune disease-afflicted relative. Children with a genetic susceptibility to type 1 diabetes were diagnosed earlier (mean age SD: 6.766±3.75 years) Autoimmunity in the patient's family was not linked to fasting c-peptide levels. Patients from autoimmune disease-prone families were more likely to get a positive GADA autoantibody test result. Children with an autoimmune first-degree relative were more likely to have an autoimmune condition (p = 0.016). This was true even if the youngster lacked autoimmunity. Taken together, 62% of type 1 diabetic children had a family history of autoimmunity. Type 1 diabetes and autoimmune thyroiditis most often afflict families. These individuals tended to be younger, have higher pancreatic autoantibody levels, and suffer more autoimmune disorders (Kossiva *et al.,* 2022).

3. Clinical Considerations of T1D

Approximately more than 650000 children are diagnosed with T1D per year. It has been estimated that over 422 million people throughout the world are living with diabetes, a chronic condition that is defined by high blood glucose (World Health Organization, 2022). This number is expected to continue to grow. Beta cells are targeted for destruction by the immune system in type 1 diabetes (T1D). T1D, which is more common in children but can also occur in adults, accounts for 10–15% of all cases of diabetes. The prevalence of type 1 diabetes in those under the age of 20 grew by 21% between 2001 and 2009 (Dabelea *et al.,* 2014), and it is projected that 5 million people in the United States will have the condition by 2050 (Dabelea *et al.,* 2014).

Diabetic ketoacidosis (DKA) is the initial indication of diabetes. Due to its severe side effects, including as electrolytic difficulties, cerebral edema, and coma (Usher *et al.,* 2012), diabetes is often the

leading cause of mortality at the time of diagnosis. DKA is often diagnosed at disease onset (Katzav *et al.,* 2014). DKA also reduces c-peptide levels due to beta cell dysfunction (Cesur and Sayin, 2013). C-peptide regulates blood sugar. DKA can occur at any stage of diabetes and is associated with poor glycemic control, neurocognitive deficits, and increased medical costs (Shalitin *et al.,* 2017). Children without a family history of type 1 diabetes or other autoimmune illnesses are more likely to experience severe DKA as their initial symptom (Klingensmith *et al.,* 2008).

4. The Relationship between Autoimmunity and T1D

Autoimmune responses to beta-cell autoantigens cause type 1 diabetes (T1DM). Insufficient insulin production is the main symptom of type 1 diabetes. Diabetes type 1 children and adolescents may develop organ-specific multiple autoimmunity as part of autoimmune polyendocrine syndrome types 1, 2, or 3. Autoimmune thyroid disease is the most common autoimmune ailment in type 1 diabetics, followed by celiac disease, autoimmune gastric disease, and others. Autoimmune thyroid disease occurs most often. Autoimmunity, especially different types, is rarely studied in children with type 1 diabetes. This study examined the categorization, prevalence, pathophysiology, predictive variables, and clinical presentation of pancreatic autoimmunity and related autoimmune diseases in children with type 1 diabetes. This article explains how connected autoimmune disorders affect diabetes management and patient health, as well as screening and follow-up therapy for autoimmunity (Kakleas *et al.,* 2015).

The autoimmune nature of type 1 diabetes has been demonstrated through the discovery of auto-antibodies directed against pancreatic islet cells, as well as their infiltration by T-cells, B-cells, and macrophages, in addition to the presence of cellular immunity abnormalities (Strous *et al.,* 2006). In addition, the presence of auto-antibodies directed against pancreatic islet cells has led to their infiltration by T-cells, B-cells, and macrophages (Kakleas *et al.,* 2015). These data provide evidence that type 1 diabetes is an autoimmune illness. There has been speculation that the autoimmune response can be initiated by a variety of factors, including hereditary and environmental factors (Walikonis *et al.,* 1998). In addition, autoimmunity can impact other organs, which can lead to organ-specific autoimmune disorders. Alternatively, autoimmunity can include several organs and tissues, which can lead to non-organ-specific autoimmune diseases such as rheumatoid arthritis. Both outcomes are possible. Autoimmune thyroid disease, coeliac disease, and autoimmune gastric disease are the three organ-specific autoimmune disorders that are most commonly associated with type 1 diabetes in children and adolescents. Coeliac disease is another autoimmune sickness that is associated with type 1 diabetes (Kakleas *et al.,* 2015).

It is conceivable for organ-specific autoimmune illnesses to be a part of an autoimmune polyendocrine syndrome (APS), which is a functional ailment that affects two or more glands. This syndrome is known as an autoimmune polyendocrine syndrome (APS). There are three completely different kinds of APS. The presence of Addison's disease, mucocutaneous candidiasis, and autoimmune hypoparathyroidism are the characteristics that set type 1 apart from the other two kinds of autoimmune hypoparathyroidism. Patients who have type 1 APS may, on the other hand, also show symptoms of type 1 diabetes, Grave's disease, hypogonadism, vitiligo, or pernicious anemia (Arya *et al.,* 2019). Some of the symptoms that may be related with APS type 2 are alopecia, Addison's disease, autoimmune thyroiditis, type 1 diabetes, hypogonadism, vitiligo, and myasthenia gravis. Another possible symptom is hypogonadism. In APS type 3A, type 1 diabetes is related not only with autoimmune thyroiditis and growth hormone insufficiency, but also with other abnormalities; on the other hand, in APS type 3C, type 1 diabetes is connected with psoriasis and celiac disease (Michels and Gottlieb, 2010).

Rachna and Satish (2022) conducted a study taking into consideration that juvenile diabetes is the most common endocrinological condition in children. Diabetes type 1 diagnoses are rising worldwide. Environmental and genetic predisposition induces pathogenesis. Diabetics have low insulin production or synthesis. Diabetes and other factors can induce either of these illnesses. Over two years and six months, the authors conducted a literature review on type 1 diabetes in children and a clinical audit of the point prevalence of diagnoses and their clinical correlates in patients who presented to AIIMS Rishikesh, a tertiary hospital. Type 1 diabetes cases upon presentation were used to calculate the point prevalence (April 2015 to September 2017). Type 1 diabetes mellitus was 2.88% in their study. Polyuria was 56.5%, polydipsia 34.8%, polyphagia 21.7%, and weight loss 39.1%. Presentation showed clinical characteristics. 26.1% had diabetic ketoacidosis at presentation. 94.4% of children and adolescents had elevated HbA1C values. Children with higher HbA1c levels and longer symptoms were more likely to suffer problems (Rachna and Satish, 2022).

5. Complications of Type 1 Diabetes

The severity and duration of hyperglycemia affect the risk of complications. Early detection, rigorous hyperglycemia control, and hypoglycemia prevention can reduce diabetes complications (The Diabetes Control and Complications, 1993). All primary care physicians should encourage children with polyuria, polydipsia, or a sudden weight shift to obtain random blood sugar measurements (Majaliwa *et al.,*

2007). If needed, children with diabetes should be sent to the correct medical professionals to reduce hyperglycemic and hypoglycemic fluctuations. Due to self-testing, injection site lipodystrophy, and hypoglycemia, insulin therapy may cause psychiatric or behavioral issues. Insulin therapy may cause injection-site lipodystrophy (Demirel *et al.,* 2013).

Microvascular disorders like retinopathy and nephropathy develop with time. Macrovascular problems include cerebrovascular, coronary, and peripheral vascular disorders. Neuropathies can affect the autonomic, peripheral, and central nervous systems. Numerous studies have found that the longer a person has poorly controlled diabetes, the higher the risk of complications (Mayer-Davis *et al.,* 2012; Salardi *et al.,* 2012).

Siafarikas and O'Connell (2010) conducted a study in the light of the fact that 15–67% of newly diagnosed T1DM patients have diabetic ketoacidosis (DKA). Seventy-nine percent consult their primary care physician first. Diabetics risk death from diabetic ketoacidosis. Cerebral oedema causes this in 0.4 to 3.1% of patients, depending on severity. The researchers aimed to improve the early detection and treatment of diabetic ketoacidosis (DKA) in non-specialist settings. Early clinical signs improve diabetic ketoacidosis diagnosis. Polyuria and polydipsia are symptoms (DKA). Urinalysis and "fingerprick" blood glucose and ketone tests are essential for early diagnosis of type 1 diabetes. Monitor ketone levels too. This is especially true in DKA-risk conditions. This prevents life-threatening complications and death. If a patient has type 1 diabetes or diabetic ketoacidosis, they must be referred to a specialist immediately. Before transferring the patient to a specialist, DKA must be carefully managed. Before transferring to a specialist, several steps must be done.

6. Management of T1D

Long and Buckner (2022) conducted a study on clinical treatment of T1D. T1D causes the loss of pancreatic beta cells, which produce insulin. Hereditary risk, islet autoantibodies, and autoreactive T cells lead to clinical illness. Natural history studies and clinical trial-linked mechanistic research have illuminated the immune system's role in sickness. In this article, the researchers reviewed the fundamental causes of type 1 diabetes, focusing on immune cell types that have been linked to the progression from presymptomatic to clinical diagnosis to established illness. The researchers also focused on immune cell types linked to the transition from presymptomatic to clinical diagnosis to established illness.

Insulin **s**hortage is a symptom of type 1 diabetes, which is caused by the immune system's destruction to the beta cells that reside in the pancreatic islets. This article provides an overview of the immunological mechanisms underpinning disease etiology as well as promising therapeutics for the treatment and prevention of type 1 diabetes. Autoimmune illness describes type 1 diabetes. The elimination of beta cells is eventually caused by the immune system's identification of the cells and the subsequent inflammation. However, similar to the progression of other autoimmune illnesses, this process takes place over the course of time and is a reflection of a number of factors that lead to clinical disease. Research into the natural history of type 1 diabetes has provided some insight into this process. It is now evident, based on research that has been conducted over a period of many years, that type 1 diabetes is caused by a convergence of genetic predisposition, environmental factors, and the maturation of B- and T-cell autoreactivity toward the beta cell and the molecules that it produces. The discovery that individuals with a first-degree relative have an increased risk of developing type 1 diabetes (T1D), in part because of human leukocyte antigen (HLA) Class II-associated genes, and the subsequent work defining the natural history of islet autoantibodies in people who are considered to have an increased risk of developing T1D (Ziegler *et al.,* 2013; Steck *et al.,* 2015) are two of the most important factors that have contributed to the advancement of our understanding of how the disease progresses. This was made possible by developments in assays that measure islet autoantibodies, either individually or as a composite. These assays include those that target insulin autoantibodies (IAA), tyrosine phosphatase (IA-2), glutamic acid decarboxylase (GADA), and zinc transporter (ZnT8) (So *et al.,* 2021). It has now been conclusively proven, using these assays in various longitudinal prospective cohorts, that the presence and amount of islet autoantibodies can be used to predict the development of clinical Type 1 Diabetes (Ziegler *et al.,* 2013; Steck *et al.,* 2015). Because of this knowledge, it is now possible to stage pre-symptomatic T1D up until the time of clinical diagnosis. Stage 1 is defined by two or more islet autoantibodies with normoglycemia, Stage 2 is defined by two or more islet autoantibodies with dysglycemia, and Stage 3 is clinical diagnosis with symptomatic T1D (Insel *et al.,* 2015). The way we think about the diagnosis of type 1 diabetes, potential treatment options, and the etiology of the disease has been fundamentally altered as a result of this staging system for the condition. However, there are still a number of important questions that need to be answered. In particular, we need to improve our understanding of the pathogenic mechanisms that promote progression through each of the stages of type 1 diabetes, and we also need to determine whether or not these mechanisms are present in all subjects with type 1 diabetes. Once we have this knowledge, we can use it to advise more specific therapy based on the stage of the disease and the type of patient.

Type 1 diabetes immunopathology and mechanisms research can use many existing methods.

These instruments include the NOD mouse model of spontaneous autoimmune diabetes. Humanized mouse models, cross-sectional, and longitudinal human cohorts are other examples of this type of technology. We review recent longitudinal and cross- sectional human research in this article. These studies are helping us comprehend the illness and its progression (Long and Buckner, 2022).

Increased T- and B-cell responses to islet antigens, poor immunological regulation, and abnormal innate inflammation disturb homeostasis and immune function predispose to type 1 diabetes. Type 1 diabetes is complicated since age, antibody–antigen specificity, and genetics are risk factors. Both experiments in this article illuminate this junction of innate and learned behavior. The first study to evaluate cross-sectional and longitudinal at-risk cohorts indicated that siblings of type 1 diabetics had greater levels of early innate inflammation and lost immunoregulatory mechanisms before clinical diagnosis (Chen *et al.,* 2014). First to assess cross-sectional and longitudinal at-risk cohorts. In a recent study, innate inflammation activates natural killer (NK) cells, which reduces regulatory T cells (Dean *et al.,* 2020).

Insulin replacement therapy is the best type 1 diabetes treatment, even though it wasn't tested on humans until 1922. Insulin therapy has been improved over the years as a result of the introduction of different kinds of insulin. These categories include short-, intermediate-, and long-acting forms of insulin, in addition to the usage of insulin that is a mixture of numerous types. Recent developments in insulin delivery have advanced the area. The development of insulin delivery pens, insulin pumps, glucose monitors, and closed loop devices, which are also known as artificial pancreas, has made it feasible for these improvements to take place. A recent clinical trial demonstrated that the closed loop system, which comprises of an insulin pump and continuous glucose monitoring, reduced the frequency of severe hypoglycemia events in hypoglycemic-prone adults who had type 1 diabetes. Insulin pumps and glucose monitors make up the closed loop system. These advances have improved glucose levels and quality of life for many type 1 diabetics (Long and Buckner, 2022).

7. Celiac Disease (CD) and Type 1 Diabetes

Celiac disease (CD) and type 1 diabetes are linked autoimmune diseases due to their similar heritage. Gluten intolerance characterizes T1D and CD. DQ2 and DQ8 molecules of the HLA genotype have this genetic basis. T1DM and CD, two of the most well-known autoimmune diseases, are linked. Several studies have linked autoantigens to early or late cereal consumption in the first months of birth or viral infections. Genetics also contributes to this issue. CD is often misdiagnosed because most patients have no symptoms. This has led to late effects like diminished height and height increase, delayed puberty, and anemia. Nephropathy and retinopathy are also linked to chronic obstructive pulmonary disease. High-risk type 1 diabetics should be screened for CD. This is done to evaluate their joint management. Gluten-free diets may improve glycemic management or reduce hypoglycemic episodes in type 1 diabetics. It may also prevent late intestinal mucosal injury, a CD consequence. Gluten causes most autoimmune reactions. This research examined the etiology, clinical overlaps, screening, and treatment of type 1 diabetes and Crohn's disease (Monar *et al.,* 2022).

8. Autoimmune Thyroid Dysfunction and T1D

Sharma *et al.,* (2022) conducted a study in the light of the fact that autoimmune thyroid dysfunction (AITD) affects all ages. Multiple autoimmune diseases can impact one patient or family. This research sought to investigate if persons with autoimmune thyroid difficulties also had Type 1 diabetes or other autoimmune diseases. The research team examined 500 AITD patients who reported to a tertiary care institution in a cross-sectional study to establish the frequency of concomitant autoimmune illnesses. 130 had Graves' disease, 370 had Hashimoto's thyroiditis. This study examined AITD prevalence and autoimmune diseases. Graves' disease had 18.5% of Type 1 diabetes and other autoimmune illnesses, while Hashimoto's thyroiditis had 27.8%. Celiac illness (8.8%) and type 1 diabetes (7.8%) co-occurred most often. 6.9% of Graves' patients and 9.5% of Hashimoto's thyroiditis patients had celiac disease. Graves' disease caused 3.1% of type 1 diabetes, while Hashimoto's thyroiditis caused 9.5%. Most non-endocrine autoimmune diseases were rheumatoid arthritis. Female sex and AITD duration over five years were associated with related autoimmune diseases. The researchers concluded that autoimmune thyroid dysfunction patients were more likely to have other autoimmune disorders. Patients who develop new symptoms or continue to have symptoms after treatment should be tested for autoimmune disorders.

9. Clinical Symptoms Associated with T1D

Patel *et al.,* (2022) conducted a study to describe public outpatient diabetes clinic treatment and referral methods for patients over 25 with T1D. In 2017, endocrinologists in one Australian urban public outpatient setting saw older type 1 diabetics in a retrospective cohort analysis. Endocrinologists examined all subjects. A modified dataset from the 2015 UK National Institute for Health and Care Excellence guidelines was used to examine paper and electronic medical records. The Australian National Diabetes Audit reported 8.5%/69 mmol/mol, however the mean HbA1c of 111 type 1 diabetics (mean age 41 13 years, 55% men, mean body mass index 27.1 5.6 kg/m2) was 8.1 1.9% (66 19 mmol/mol). 25.5% of participants met the guideline threshold of 53

mmol/mol (7.0%), the percentage of type 2 diabetics. After complication screening, 80.2% of patients have seen a diabetes educator or dietitian (73.0%). Ischemic heart disease or myocardial infarction affected 10.5% of patients, peripheral neuropathy 30.1%, nephropathy 20.4%, and retinopathy 27.4%. 27% of referrals followed acute inpatient admission or emergency room visit, and 13% were for diabetes care in pregnant patients. Taken together, when pregnant or hospitalized for acute glycemia, many type 1 diabetics sought public specialist treatment. Acute glycemia-related hospital presentations were avoidable in most cases. Aftercare meets all national specialized norms. The neighborhood's interdisciplinary expert service receives few recommendations because this region uses "wait for acute event" rather than "complication prevention" care. Urgent effort is needed to better understand the incidence of this treatment and how to reduce it.

T1D is a lifelong autoimmune disease that requires a specialist team to treat (Comprehensive Medical Evaluation and Assessment of Comorbidities, 2020). The condition increases morbidity and death, lowering birth life expectancy by 12.2 years (Huo *et al.*, 2016). Diabetics type 1 are hospitalized more often (McIntyre *et al.*, 2010). This applies to many diseases, including diabetic ketoacidosis acidosis (DKA) and others (such as infections) (McIntyre *et al.*, 2010).

Self-management and quality treatment, including structured diabetes education, can reduce hyper- and hypoglycemia-related acute hospital and emergency department (ED) visits (DCCT, 1993; Elliott *et al.*, 2014). Hyper- and hypoglycemia cause this. Long-term hyperglycemia problems can be reduced by interdisciplinary teams that monitor and control glycemia (Elliott *et al.*, 2014). Managing blood pressure and lipids can minimize the risk of cardiovascular diseases in both the macrovascular and microvascular systems (Nathan *et al.*, 2014). Type 1 diabetes guidelines defined these therapeutic criteria. These guidelines emphasize self-management, patient education, and routine complication screening to attain treatment targets. These guidelines also stress routine complication screening for primary prevention (Patel *et al.*, 2022).

10. CONCLUSION

Patients diagnosed with type 1 diabetes who present to the emergency room typically have acutely elevated blood glucose levels. Patients who fit this profile typically suffer from additional autoimmune conditions, such as thyroid disease and celiac disease, which need to be taken into account. The staff members who work in the emergency department should be adequately prepared to think in a holistic manner so that they can take the appropriate steps in diagnosing autoimmune diseases through the management of patients who have type 1 diabetes.

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