Risk factors for type 1 diabetes mellitus in children live in Karbala province-Iraq.

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Abstract

Background: The most important autoimmune disease which affects children is Type 1 Diabetes Mellitus (T1DM). The main risk factor for this chronic condition is genetic that contributed to loci within the HLA complex. Even, the environmental issues triggering the disease are still unclear so this study aimed to identify the most important risk factors related to type 1 diabetes mellitus among children and adolescents.

Methods: This is a descriptive cross-sectional study conducted among 50 confirmed diabetic children and adolescents visiting AL-Hussainy hospital in Karbala. Time of data collection continuous for two month *i.e.* July and August 2019. After consenting for voluntary participation in the study, parents were answering a special questionnaire containing demographic and risk factors data.

Results: The age range of participate diabetic children was (18 months-17 years), around 70% of patients have never had a family history of diabetes and only 32% mentioned having thyroid diseases among their relatives. Analysis of the related maternal risk factors was showing the majority (84%) was drinking tea during pregnancy; no one had a smoking history. Only 6% diagnosed with gestational diabetes and 3% were treated with insulin. Regarding factors associated with the neonatal period, all children were delivered in the hospitals and 68% of these deliveries were normal and more than half 54% had no disease during their neonatal life. Most of the participant children (80%) continued their breastfeeding for more than 6 months.

Conclusion: there are a lot of environmental risk factors related to pregnancy, neonatal period, and early childhood widely distributed among patients with type 1 DM and may have their role in causing diabetes among those patients.

Introduction

Children around the world can be presented and diagnosed with Type 1 Diabetes Mellitus (T1DM) which is one of the genetically contributed autoimmune diseases that activated by different environmental factors. These factors are still not completely known. There are different immunological theories for the development of T1DM but the key role is for loci within the Human Leukocyte Antigen (HLA), especially class II. Even though recent studies were reached to significant information about the etiology of this disease but there still increasing in the diagnosis of new cases by 3-5% per year with a high mortality rate [1,2].

In addition to the genetic predisposition of T1DM, it is of great importance to distinguish the unknown environmental factors associated with the occurrence of T1DM such as particular food types or infection with special types of viruses that induct the autoimmune activity causing damage to Beta Cells (B-cell) of the pancreas and resulting in T1DM [3-5].

These environmental factors are different from person to person and place to place because of the difference in genetic and risk exposure. There are some types of viruses that have proved their role in causing T1DM like rubella, mumps, cytomegalovirus, and coxsackie B-virus by infection to pancreatic B-cells [4,7,8].

Some dietary issues have also been proved to have a role in causing B-cell defect and finally leading to T1DM even with unknown mechanism. Other factors related to the development of diabetes among young children are greatly linked to the in-utero life and maternal related issues [9-11].

Knowing the causative environmental factors related to the pathogenesis of T1DM is very helpful for prevention and disease control in addition to decrease health expenditures required for dealing with the disease. Lots of these factors are preventable in different levels by prevention to exposure to the risk factor (primary prevention) or by controlling the damage progression before any clinical symptoms and complications developed (secondary prevention).

So, the current study was conducted to identify the distribution of potential risk factors related to type 1 DM including maternal, neonatal, and early childhood factors [11,12].

Patients and Methods

Study design and duration

This is a descriptive cross-section study conducted during the period from the beginning of July to the end of August 2019.

Study population and sample

This study was carried on a sample of 50 children and adolescents with T1DM who have been consulting to the pediatric endocrinology unit at Al-Hussiany hospital in Karbala province.

All patients diagnosed with T1DM and less than 18 years old were visiting the specialist unit in the hospital during the determined period of data collection were included.

Data collection and questionnaire

Parents and accompanying relatives of the involved patients were consented to participate in answering the special questionnaire proposed for this study.

The questionnaire consisted of the following information: part one contains some demographic data like age, gender, any family history of DM and whether it is T1DM or Type 2 Diabetes Mellitus (T2DM), presence of other autoimmune diseases among family members (first and/or second degree).

Part two contains questions related to different risk factors that may be contributing to the disease etiology including both

maternal (habits, drugs, and diseases) and neonatal (diseases and delivery conditions). In addition to any related childhood disease or infection.

Ethical considerations

The required agreement to deal with patients in the hospital was obtained from Karbala Health Directorate while the ethical approval was obtained from the ethical committee in College of Medicine/Wasit university. All data obtained from participant patients were kept confidential and used only for the research purpose.

Statistical analysis

Collected data were analyzed by SPSS software program version 24, using frequency and percentages for categorical data while age was presented by mean ± standard deviation.

Results

During the predetermined period for data collection, only 50 diabetic children were visiting the chosen endocrine unit in the hospital. The age range of those patients was from 18 months to 17 years old.

The remaining demographic features of the patients are displayed in Table 1. The majority of the patients were females (70%). Most of the patients 38 (76%) were using multiple injections of insulin while the remaining 12 (24%) were using twice injection.

Characteristic variables	Frequency and percentages
Male	15 (30%)
Female	35 (70%)
Age of patients	
Age range	18 months-17 years
Age mean ± standard deviation	9 ± 2.3
Insulin regimen	
Twice daily	12 (24%)
Multiple daily injections	38 (76%)

Table 1. Demographic features of children patients with type 1 diabetes mellitus.

Table 2 shows the data relating to the family history of autoimmune diseases. The majority of them (60%) expressed no family history of any type of diabetes among both first- and second-degree relatives. Type 1 DM was mentioned among 12

(24%) while only 2 (4%) mentioned both types 1 and 2. Even half of the patients had no family history of other autoimmune diseases; thyroid diseases represented the highest percentage among the remaining half with about 16 patients (32%) followed by (10%) for celiac disease.

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Family history of diabetes mellitus	Frequency and percentages
No disease	30 (60%)
T1DM*	12 (24%)
T2DM**	6 (12%)
Both T1DM +T2DM	2 (4%)
Family history of other autoimmune diseases	
No disease	25 (50%)
Thyroid diseases	16 (32%)
Celiac disease	5 (10%)
Pernicious anemia	0%
Vitiligo	4 (8%)

Table 2. Frequency distribution of family history of related autoimmune diseases. *: Type 1 diabetes mellitus; **: Type 2 diabetes mellitus.

Mother habits during pregnancy show that 42 (84%) of them keep drinking tea during the pregnancy period. Only 3 out of 50 (6%) mentioned gestational diabetes and no one had an autoimmune disease. When asking women about the ingested drugs during pregnancy, around 36% of them said they didn't take any type of drugs while 18%, 13%, and 9.4% mentioned taken anti-emetic, antihypertensive, and antibiotics respectively as shown in Table 3.

Maternal habits during pregnancy	Frequency and percentages
Smoking habits	0 (0%)
Tea drinking	42 (84%)
Coffee drinking	8 (16%)
Maternal diseases	
No diseases	34 (68%)
Pre-eclampsia	8 (16%)
Gestational diabetes	3 (6%)
Autoimmune diseases	0 (0%)
Infectious diseases	5 (10%)
Drug history during pregnancy	
No any drugs	18 (36%)
Antibiotics using	6 (9.4%)
Analgesics drugs	3 (5.2%)
Antihypertensive drugs	9 (13%)
Anti-emetic drugs	11 (18%)
anti-epileptic	0 (0%)
insulin	3 (3%)

Table 3. Maternal risk factors related to pregnancy.

The risk factors related to delivery were presented in Table 4 and shows all deliveries were performed at hospitals and most of them were normal vaginal (68%). More than half (54%) of the diabetic children never had any disease during the neonatal period while less than a third (28%) of them had jaundice during that period.

Place and mode of delivery	Frequency and percentages
Normal vaginal delivery in hospital	34 (68%)
Ceserian section in hospital	16 (32%)
Normal vaginal delivery in home	0 (0%)
Neonatal disease	
No disease	27 (54%)
Respiratory disease	5 (10%)
Jaundice	14 (28%)
Other neonatal infections	4 (8%)

Tabel 4. Risk factors related to the neonatal period.

The majority (80%) of the participated diabetic children in this study had breastfed for more than six months but 36 (70%) received weaning food before they complete their sixth month of age as appears in Table 5.

Feeding history	Frequency and percentages
Duration of breastfeeding	
Less than 6 months	10 (20%)
More than 6 months	40 (80%)
Age of adding food with the milk	
Less than 6 months	35 (70%)
More than 6 months	15 (30%)

Table 5. Dietary related risk factors.

In Table 6, the frequency distribution of the most presenting symptoms among patients shows (70%) was presented with unusual frequent urination, and (50%) with polydipsia. Diabetic Ketoacidosis (DKA) was the presentation of 9 patients (18%) only.

Symptoms	Frequency and percentages
polyuria	35 (70%)
polydipsia	25 (50%)
weight loss	15 (30%)
DKA* at presentation	9 (18%)

Table 6. Presenting symptoms among type 1 diabetes mellitus children. *Diabetic Ketoacidosis.

Discussion

As the identification of the possible risk factors distribution among patients with T1DM is a very important issue in preventing medicine, so this study was conducted to define the most frequent risk factors related to patients presented with this disease. Karbala province in special had no similar type of these studies so we perform this research to define environmental factors related to pregnancy, neonate, and feeding habits of T1DM patients during early childhood which may contribute to their disease. Family history of both DM types was presented among 40% of the children. The history of T1DM among patients' relatives was more frequent than Type 2 Diabetic Mellitus (T2DM). Previous studies found a significant association between being diabetic and a family history of T1DM while another study found no relation with a family history of T2D [14-16]. Even, it was confirmed that both T1DM and T2DM can present in members from the same family due to genetic predisposition for those family members related to specific mediated phenotype and insulin resistance [17-18].

This study found that thyroid diseases were the most frequent autoimmune disease presented among first and second-degree relatives of the patients. This was confirmed by a study done in Kuwait that found a significant association between T1DM and thyroid diseases [16]. This result may be explained by the identical genetic pathogenesis represented by (HLA-DR3) which making them occur mutually [19]. Besides the presence of CTLA-4 + 49 A/G and CT60 gene polymorphism which is of high susceptibility to T1DM, mainly with autoimmune thyroid disease patients [20].The tea-drinking was frequently reported among mothers during the pregnancy of the participant diabetic child which was previously reported by another study [6]. Similar to our study, it was found that special types of maternal disease can

be considered as risk factors for T1DM like pre-eclampsia and infections during pregnancy [21-23]. It is an unknown mechanism by which the diseases and complications occurring during pregnancy can effect on fetus's immune system development [22]. Another study in Norway was disagreed and found no significant association between pregnancy complications and fetus susceptibility to T1DM [24]. Even that infection during pregnancy may be a significant environmental stimulator for T1DM, a lot of studies reported particular types of infection like rotavirus infection or enter viruses during fetal life or infancy also have a great role in developing the disease [9,25]. This is considered as one of the neonatal problems related to the development of T1DM like respiratory distress and jaundice [21,26]. Neonates with jaundice related to blood group incompatibility were found to be more susceptible to T1DM by unidentified mechanism in addition to jaundice occur just after birth that may be explained by exposure to phototherapy [21]. Even so, a previous study in Scotland found T1DM not related to elevated blood pressure, type of delivery, feeding mode, and even neonatal jaundice [27,28]. Few percentages of patients with T1DM in this study were mentioned infection with respiratory or other types of infections during the neonatal period while it was higher among diabetic patients in another study conducted in Sweden which was compatible to result obtained from experimental studies on animals that found different ways for developing T1DM due to infection by B-cell lysis, by alteration or stimulation auto-reactive T-cell and molecular mimicry [29,30].

Although exclusive breastfeeding for the first six months known to be an important factor to prevent lots of diseases and infections in later life especially diabetes by adjustment of B cells autoimmune risk, this study showed a higher percentage of patients who diagnosed with T1DM had a history of breastfeeding for more than 6 months but most of them were not exclusive and were receiving weaning food before the age of six months. This study was a descriptive study with a lot of limitations; one of them is the unavailability of a control group from the non-diabetic children to make a comparison between them.

Conclusion and Recommendations

Patients with T1DM expressed higher percentages of different environmental factors that may be contributed to their diseases. Some of these factors were related to in utero life during pregnancy like (maternal drinking of tea, gestational diabetes, and pre-eclampsia), other factors related to early life as (infection and jaundice). This study recommends screening for other related modifiable environmental risk factors, besides; avoid exposure to these factors to prevent the development of T1DM among children.

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