# Risk Factors of Type 1 Diabetes Mellitus in Children below Five Years

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## ABSTRACT

**Background:** Type 1 diabetes mellitus is a chronic autoimmune disease that affects people with underlying genetic predisposition. It is thought to be brought on by environmental triggers that have not been discovered yet.
**Objectives:** To find out the risk factors of type 1 diabetes in children below five years old.
**Methods:** A case control study that was conducted in Central Child Teaching Hospital during a one year period, from 1st of January to 31st of December 2020. The study included 300 patients aged < 5 years divided into two groups: Case group included 100 patients aged < 5 years with newly diagnosed type 1 diabetes mellitus and control group included 200 patients aged < 5 years attended the outpatient clinic for complains other than diabetes.
**Results**: In this study, the mean age of patients was 2.35 (±1.26) years. Regarding age and gender, both was not significantly associated with type 1 diabetes. The highest proportion of children who was newly diagnosed with type 1 diabetes were living in urban area (41.3%, P= 0.001), those with BW ≥ 2.5 kg (38.2%, P= 0.009), in term babies (45.4%, P= 0.001), who had positive family history of DM (P= 0.046 and all of them were 1st degree relatives), those with bottle type of feeding (58.9%, P= 0.001). The highest proportion of cases was diagnosed in spring and autumn months (14% and 10% in March and April, respectively; and 12%, 10%, and 13% in September, October and November, respectively). The majority of case group (61%) had moderate to severe deficiency of vitamin D.
**Conclusion:** The current study identifies six factors to have a significant associate with type 1 diabetes in children below five years of age these includes: Residence in urban area, birth weight ≥ 3.5 kg, delivery at term, positive family history of diabetes, bottle feeding and vitamin D deficiency).
**Keywords: Type 1 diabetes, Risk factors, Children, Iraq.**

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Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease that affects people with underlying genetic predisposition. T1DM is thought to be brought on by environmental triggers that have not yet been discovered[1]. Although the exact etiology of type 1 diabetes mellitus is undefined[2], there is genetic and different environmental factors have been identified, there is clear familial clustering of TIDM with prevalence in sibling approaching 8%, the risk is 3-4% if the mother is affected but 5-6% when the father is affected.

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Environmental risk factors include (during pregnancy (tea drinking, pre-eclampsia, and infectious diseases), neonatal period (respiratory distress, jaundice and infections), and early infancy nutritional, viral infection, body mass index and vitamin D deficiency) are considered as potential triggers for T1DM development in children.[3,4]

Identifying risk factors for T1DM play an important role in prevention and modulation of the disease process[5]. However, risk factors for development of T1DM in children less than 5 years of age is inadequately studied, so this study aimed at identifying risk factors for development of T1DM in children of less than 5 years of age.

## Methods

This was a case control study that was conducted in the emergency room, counseling clinic and outpatient clinic of Central Child Teaching Hospital during the period of one year from 1st of January till end of December 2020. The study included 300 patients aged < 5 years who admitted to the emergency room or outpatient clinic and divided into two groups. Group 1 Included 100 patients aged < 5 years with newly diagnosed type 1 diabetes mellitus. Group 2 included 200 patients aged < 5 years attended for complain other than diabetes. Diagnosis of DM was depending on basis of typical symptoms (polydipsia, polyuria, weight loss), and laboratory data fasting plasma glucose level at or above 7.0 mmol/l (126 mg/dl) and/or plasma glucose at or above 11.1 mmol/l (200 mg/dl)[6]. Demographic information was collected from relative of patients such as age and gender, residence, type of feeding, family history of DM, birth weight, gestational age at delivery. Duration of symptoms and month of diagnosis, preceded infection. Recording of vitamin D level status.

The data analyzed using Statistical Package for Social Sciences (SPSS) version 25.A level of P – value less than 0.05 was considered significant.

## Results

The total number of study patients was 300. They were divided into two groups: Case group included 100 patients below five years old with newly diagnosed T1DM, and control group included 200 patients below five years old who were attended the hospital for other complaint. Regarding the age and gender, there were no significant differences in age and gender between study groups (p value = 0.138**,** 0.412) consecutively, (Tables 1 and 2).

Four factors were found to be statistically significant in children with newly diagnosed type 1 DM: residence in urban area (p value =0.001), having birth weight ≥ 3.5 kg (P= 0.009), delivered at term (P= 0.001), those with bottle type of feeding (58.9%, P= 0.001), (Table 2).

Table 3 shows the distribution of case group by certain characteristics. The highest proportion of cases was diagnosed in spring and autumn months (14% and 10% in March and April respectively; and 12%, 10%, and 13% in September, October, and November respectively). Regarding recent infection, 25% of case group mentioned a recent history of UTI. Duration of symptoms was within one week in 63% of the patients.

The majority of case group had moderate to severe deficiency of vitamin D (61%), (Table 4).

**Table 1: Comparison between study groups by age and gender.**

| Variable | Study Group | | P – Value |
|---|---|---|---|
| | Case n= 100 | Control n= 200 | |
| Age (year) Mean ± SD | 2.49 ± 1.25 | 2.24 ± 1.28 | **0.138** |
| Gender. n. (%)<br>Male<br>female | <br>57 (57)<br>43 (43) | <br>104 (52)<br>96 (48) | 0.412 |

**Table 2: Association of certain clinical information and type 1 diabetes.**

| Variable | Study Group | | Total (%) n= 300 | P – Value |
|---|---|---|---|---|
| | Case n= 100 | Control n= 200 | | |
| **Residence** | | | | |
| Urban | 69 (41.3) | 98 (58.7) | 167 (55.7) | **0.001** |
| Rural | 31 (23.3) | 102 (67.7) | 133 (44.3) | |
| **Birthweight (Kg)** | | | | |
| < 2.5 | 23 (23.2) | 76 (76.8) | 99 (33.0) | **0.009** |
| 2.5 -3.5 | 27 (25.23) | 80 (74.77) | 107 (35.67) | |
| >3.5 | 50 (53.19) | 44(46.81) | 94 (31.33) | |
| **Gestational age at labor** | | | | |
| Term | 89 (45.4) | 107 (54.6) | 196 (65.3) | **0.001** |
| Preterm | 11 (10.6) | 93 (89.4) | 104 (34.7) | |
| **Family History** | | | | |
| No | 25 (44.6) | 31 (55.4) | 56 (18.7) | **0.046** |
| Yes | 75 (30.7) | 169 (69.3) | 244 (81.3) | |
| **Feeding** | | | | |
| Breast | 16 (16.5) | 81 (83.5) | 97 (32.4) | **0.001** |
| Mixed | 31 (27.4) | 82 (72.6) | 113 (37.3) | |
| Bottle | 53 (58.9) | 37 (41.1) | 90 (30.3) | |

**Table 3: Distribution of case group by certain characteristics.**

| Variable | | No. (n= 100) | Percentage (%) |
|---|---|---|---|
| **Season and Month of diagnosis** | | | |
| Winter | Dec. | 4 | 4.0 |
| | Jan. | 7 | 7.0 |
| | Feb. | 3 | 3.0 |
| Spring | Mar. | 14 | 14.0 |
| | Apr. | 10 | 10.0 |
| | May. | 7 | 7.0 |
| Summer | Jun. | 8 | 8.0 |
| | Jul. | 6 | 6.0 |
| | Aug. | 6 | 6.0 |
| Autumn | Sep. | 12 | 12.0 |
| | Oct. | 10 | 10.0 |
| | Nov. | 13 | 13.0 |
| **History of Recent Infection** | | | |
| No | | 55 | 55.0 |
| UTI | | 25 | 25.0 |
| URT | | 20 | 20.0 |
| **Duration of symptoms (day)** | | | |
| ≤ 7 | | 63 | 63.0 |
| > 7 | | 37 | 37.0 |

UTI: Urinary tract infection, URT: Upper respiratory tract infection.

**Table 4: Vitamin D status in patients with newly diagnosed type 1 diabetes.**

| Vitamin D Status | No. (n= 100) | Percentage |
|---|---|---|
| Moderate to severe deficiency (<20nMol/l) | 61 | 61.0 |
| Mild deficiency (20-29) nMol/l | 37 | 37.0 |
| Normal (>30nMol/l) | 2 | 2.0 |

## Discussion

The current study revealed that mean of age was 2.35 (±1.26) years, a finding similar to that reported by Al-Fifi et al study in 2010[7]. There were no significant differences in age and gender between study groups (P ≥ 0.05) which agree with studies by Waernbaum et al[8] and Saad et al[9]. In this study, the highest proportion of children with newly diagnosed T1DM was seen among those who are living in urban area (P= 0.001), this could be explained by the hygiene hypothesis states that T1DM is a disease of industrialized countries, and increase awareness and educational level among population in urban area.

Majority of children with newly diagnosed T1DM in this study were found to have birth weight ≥ 3.5 kg (P= 0.009), this match results of Goldacre et al study in 2018, who observed that children born at higher than average birthweight (3500-3999 g or 4000-5499 g) had a higher incidence of T1DM[10]. In addition, Cardwell et al study observed that children with birthweight >4 kg had an increased risk of T1DM compared with children weighing 3.0–3.5 kg at birth[11]. According to gestational age at delivery highest proportion in term babies (45.4%, P= 0.001).

This study revealed a significant relation between those who had positive family history of DM and new diagnosis of T1DM (44.6%, P= 0.046 and all of them were 1st degree relatives), which agreed to the results observed in Majeed et al study in 2011, in which the risk of T1DM was significantly associated with the occurrence of T1DM (either alone or in addition to family history of T2DM) in first and second degree relatives [12].

A significant relation between children with newly diagnosed T1DM and bottle type of feeding (58.9%, P= 0.001) and this agree with result of study conducted by Lund-Blix and other co-authors in 2017, they found that children who were never breastfed had a twofold high risk of T1DM compared with those who breastfed. Among those who were breastfed, the incidence of T1DM was independent of duration of both full breastfeeding and any breastfeeding[13]. Feeding pattern in early life (as breast, cow milk or mixed feeding) and its duration were assessed in Majeed et al study and showed that breast feeding less than six months is an important factor among children with newly diagnosed T1DM [12].

The current study revealed that highest proportion of children with T1DM was diagnosed in spring and autumn months (14% and 10% in March and April respectively; and 12%, 10%, and 13% in September, October, and November, respectively). A similar finding noticed in Gerasimidi et al study in 2016, in which analysis by month revealed significant seasonality, with January being the month with the highest and June with the lowest percentage of incident cases (P < .001). Winter, early spring and late autumn months had higher percentage of incident cases compared with late spring and summer (P<0.05)[14]. Different suggestions were made to explain seasonality in T1DM diagnosis. Seasonal viral infections (as, enteroviruses, rotavirus, mumps and cytomegalovirus) have been implicated in etiology of T1DM [15].

This study found that majority of children with newly diagnosed T1DM had moderate to severe deficiency of vitamin D (61%). Liu et al in 2018 found that vitamin D deficiency is common in T1DM children[15], in addition Savastio et al study in 2016 reported that children with T1DM show a generalized

vitamin D deficiency that impact on metabolic and glycemic homeostasis[16]. Emerging evidences suggest that vitamin D insufficiency may be a risk factor for both T1DM and T2DM.

In conclusion; The current study identifies six factors to have a significant associate with T1DM in children below 5 years of age these includes: Residence in urban area , birth weight ≥ 3.5 kg, delivery at term, positive family history of diabetes, bottle feeding, vitamin D deficiency.

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