Factors Associated with Type-1 Diabetes Mellitus in Children Aged 2-15 Years: A Case-Control Study from southern Iran

Marzieh Zamani
Jahrom University of Medical Science
Vahid Rahmanian
Jahrom University of Medical Science
Samira Rezaei
Jahrom University of Medical Science
Hekmatollah Khubfekr
Iranshahr University of Medical Sciences
Azam Namdar (hila421@yahoo.com)
Fasa University of Medical Science

Research

Keywords: Type 1 diabetes mellitus, breast milk, breastfeeding, diet, children, Iran

Posted Date: February 24th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-250793/v1

Abstract

Background

This study aimed to investigate the association between Type-1 Diabetes Mellitus and diet in the first two years of life as well as a select group of demographic variables.

Methods

This case-control study was conducted on 76 children with T1DM and 209 non-diabetic children selected through convenience sampling from the population of people visiting the community health centers of the city of Jahrom, Iran. The required data were collected by a questionnaire of diet and demographic information that was completed by the mothers of the children. The data were analyzed using logistic regression and adjusted odds ratio.

Results

Finally, the results of multiple backward logistic regression showed that Body Mass Index (BMI) of the mother being less than 18.5 before pregnancy (OR: 4.4, 95% CI: 1.61 to 11.97), mothers without a history of diabetes (OR: 0.02, 95% CI: 0.001 to 0.60), mother's weight before pregnancy (OR: 0.88, 95% CI: 0.84 to 0.91), mother's excess weight during pregnancy(OR: 0.83, 95% CI: 0.75 to 0.93), exclusive breastfeeding for more than six months (OR: 0.19, 95% CI: 0.03 to 0.96), low weight gain in the first two years of life (OR: 6.98, 95% CI: 2.16 to 22.5), and the breastfeeding less than 12 months (OR: 10.52, 95% CI: 1.62 to 66.64) have association with Type 1 diabetes ($p < 0.05$).

Conclusion

Body mass index less than 18 mothers before pregnancy, Low weight gain in the first two years of life and breastfeeding less than 12 months increases the risk of developing Type-1 Diabetes in children.

Background

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease associated with the destruction of pancreatic β cells, which leads to extreme or absolute insulin deficiency. People with T1DM require lifelong insulin therapy. T1DM is a major public health problem with increasing prevalence worldwide (1, 2).

The increase in knowledge of type 1 diabetes over the past 25 years has led to a broad understanding of many aspects of the disease, including genetics, epidemiology, the phenotype of immune cells, and beta

cells and the burden of disease. Globally, type 1 diabetes is increasing in both prevalence and incidence, with an overall annual increase in occurrence of about 2–3% per year (3).

However, the incidence of type 1 diabetes varies by country and by region within countries (4). For example, at northern latitudes, people born in the spring are more likely to develop the disease than those born in the other seasons (5).

Type 1 diabetes mellitus is one of the most common chronic diseases that develops in childhood. For unknown reasons, its incidence in children increases from 3 to 5% every year worldwide (6) .The peak incidence of diagnosis is seen in children aged 10–14 years (3, 4).

On the other hand, diabetes is the most common chronic metabolic disease diagnosed in children and adolescents. Although diabetes is not contagious, it is the first and only disease that the United Nations has designated as a 21st century epidemic (6).

However, no reliable data are available on the prevalence of diabetes in many countries (7). The results of international research (DIAMOND and EURODIAB) reveal an increasing trend in Diabetes prevalence in most regions of the world, with the highest growth dynamics in the youngest age group (6, 7).

The global increase in T1DM prevalence is a well-known fact; with the highest rate reported from fast developing countries (8, 9).

Infants experience many changes in their diet in the first year of life. In many cases, their diet initially consists exclusively of breast milk, but gradually shifts from being entirely liquid (breast milk, cow milk, and formula) to also a variety of solid foods (10, 11). Research has shown that using cow milk in infancy increases the risk of β-cell autoimmunity, probably because of the similarity of the molecular sequence of cow milk proteins with the body’s own antigens (12, 13). According to several studies, introducing gluten or cereals, fruits, roots, and seeds to the food before 3 months of age is a risk factor for the autoimmunity to the islets of Langerhans (14, 15). Solid foods can also play a pathogenic role in the development of T1DM in the same way as hypothesized for cow milk (12). Some have recommended that to reduce the risk of immunodeficiency disorders, complementary foods should be added to breast milk starting from the age of 4 to 6 months (14).

However, numerous epidemiological reports have linked the increased risk of T1DM to short breastfeeding period and early introduction of cow milk, formula, or complementary foods to the baby’s diet (14, 16, 17).

It is widely recommended to continue exclusively breastfeeding for the first 4 to 6 months of the infant's life. Research has confirmed the health benefits of this breastfeeding and also continued breastfeeding during the first year of life. In any case, it is not recommended to start complementary feeding before 4 months of age (10, 14, 16, 17).

With the increasing prevalence of T1DM worldwide, the management and treatment of this disease and its acute and chronic complications are imposing significant burdens on patients as well as health care systems (18, 19). In this study, the objective was to investigate the potential relationships between T1DM and infant's diet in the first two years of life as well as some demographic variables.

Methods

Design

The present case-control study was conducted on a sample of children (aged 2–15 years old) in Jahrom, Fars Province, southern Iran in 2018. The study was approved by the Ethics Committee of Jahrom University of Medical Sciences (IR.JUMS.REC.2017.173).

Sample size and sampling

The required sample sizes were calculated using a similar study (20) with, 95% confidence level, and the required size was estimated at 285.

In this study, the cluster sampling method was used, in which each health center was considered as a cluster. At first, at each center a sequential number was assigned to all children with Type 1 diabetes. Then, regarding the proportion of participants, cases were selected randomly using the random number table. Next, controls were selected from healthy children referred to centers and matched with cases in terms of age and gender.

Case and control groups were selected considering the inclusion and exclusion criteria.

The inclusion criteria for the case group were as follows: being 2 to 15 years of age and having T1DM as reported by the mother or according to the child's health record. The inclusion criteria for the control group were as follows: being in the same age range as the case group and not having type 1 or type 2 diabetes or impaired glucose tolerance (IGT) at the time of the study. The exclusion criteria for the case group were as follows: not being in the age range of 2–15 years or not having T1DM and refusal to give informed consent.

The exclusion criteria for the control group were as follows: not being in the same age range as the case group and being diagnosed with type 1 or 2 diabetes or IGT and refusal to give informed consent.

Data collection

The data collection method was upon visiting the community health centers, the mothers of the eligible children were asked to complete a self-administered questionnaire of diet and demographic information, which consisted of two groups of questions

Instruments

1- Demographic and child nutrition status information questionnaire:

It was specifically developed based on the study objectives and contained 11 items including

Questions about the child (gender, age, duration of exclusive breastfeeding, age of onset of complementary feeding, age of complete weaning, use of formula or similar products in the first six months of life, use of pasteurized milk in the first year of life, birth weight, weight at 1 year of age, fetal age at birth, and birth order).

2- Demographic and mother pregnancy status information questionnaire:

Questions about the mother contained 5 items including age at delivery, excess weight during pregnancy, method of delivery, history of diabetes, history of diabetes among the child's other first-degree relatives.

Data analysis

After collecting the questionnaires, the obtained data were entered into SPSS Version 16.0. (Chicago, SPSS Inc.).

Normality of all data were checked by Kolmogorov-Smirnov test. For normally distributed data, the chi-square test and the t-test, and for non-normally distributed data, the Mann-Whitney test were used to compare qualitative and quantitative variables of the case and control groups. Finally, logistic regression with the backward technique was used to compute the odds ratio and the 95% confidence interval and investigate the association between T1DM and the variables.

Results

This study comprised of 285 children, including 165 (57.89%) males and 120 (42.11%) females, with 76 case and 209 as of control.

The results obtained did not reveal any significant association between child age, maternal age during pregnancy, gestational age, sex, birth weight, one-year weight, birth rank, history of diabetes in relatives, age of starting complementary feeding, consumption of cow milk under one year and use of artificial milk ($p > 0.05$) (Table 1, 2).

Table 1
Mean and standard deviation of the child's age and mother's age at delivery, weight before pregnancy, and excess weight during pregnancy in the case and control groups (univariate analysis)

Quantitative variables	Control group	Case group	p-value *
	Mean ± standard deviation		
Child's age (years) ●	11.94 ± 3.3	12.14 ± 4.13	0.69
Mother's age at delivery (years) ¥	25.58 ± 6.87	25.71 ± 5.31	0.88
Mother's weight before pregnancy (kg) ●	64.81 ± 8.81	56.62 ± 10.72	0.0001
Mother's excess weight during pregnancy (kg) ●	10.72 ± 2.91	8.92 ± 4.51	0.0001
* $p < 0.5$ is considered statistically significant.			
¥ Mean and standard deviation are obtained using the Mann-Whitney test.			
● Mean and standard deviation are obtained using the t-test.			

Table 2
Absolute frequency and distribution (percentage) of study variables in the case and control groups (univariate analysis)

Qualitative variables			Control: frequency No. (%)	Case: frequency No. (%)	p-value
Child's non-diet variables	Fetal age at birth	Less than 37 weeks	22 (10.5)	10 (13.1)	0.53
		More than 37 weeks	187 (89.5)	66 (86.9)	
	Gender	Female	90 (43.1)	30 (39.5)	0.58
		Male	119 (56.9)	46 (60.5)	
	Birth weight	Less than 2500 gr	20 (9.6)	8 (10.5)	0.81
		More than 2500 gr	189 (90.4)	68 (89.5)	
	Weight at 1 year of age	Less than 9500 gr	49 (23.4)	21 (27.6)	0.47
		More than 9500 gr	160 (76.6)	55 (72.4)	
	Birth order	First or second	143 (68.4)	57 (75)	0.28
		Third or fourth	66 (31.6)	19 (25)	
Mother's variables	History of diabetes	Yes (before pregnancy/pre-gestational)	1 (0.5)	3 (3.9)	0.07
		Yes (during pregnancy/gestational)	13 (6.2)	6 (7.9)	
		No	195 (93.3)	67 (88.2)	
	Method of delivery	Vaginal	119 (56.9)	57 (75)	0.02
		C-section	90 (43.1)	19 (25)	
	Mother's BMI	Normal	119 (56.9)	49 (64.5)	0.0001
		Underweight	16 (7.7)	18 (23.7)	
		Overweight	62 (29.7)	8 (10.5)	

Qualitative variables			Control: frequency No. (%)	Case: frequency No. (%)	p-value
		Obese	12 (5.7)	1 (1.3)	
	History of diabetes in first-degree family members	Yes	112 (53.6)	33 (43.4)	0.12
		No	97 (46.4)	43 (56.6)	
Child's diet and growth variables (in the first two years of life)	Exclusive breastfeeding	Less than 4 months	19 (9.1)	13 (17.1)	0.04
		5 months	17 (8.1)	2 (2.6)	
		6 months	65 (31.1)	30 (39.5)	
		More than 6 months	108 (51.7)	31 (40.8)	
	Status of the baby's weight gain chart during the first two years of life	Below the normal line	49 (23.4)	10 (13.2)	0.08
		Normal	146 (69.9)	63 (82.9)	
		Above the normal line	14 (6.7)	3 (3.9)	
	Age of onset of complementary feeding	Less than 4 months	7 (3.3)	4 (5.3)	0.18
		5 months	16 (7.7)	8 (10.5)	
		6 months	118 (56.5)	49 (64.5)	
		More than 6 months	68 (32.5)	15 (19.7)	
	Use of cow milk in the first year of life	Yes	20 (9.6)	12 (15.8)	0.14
		No	189 (90.4)	64 (84.2)	
	Use of artificial milk	Yes - along with breast milk	33 (15.8)	12 (15.8)	0.64
		Yes - without breast milk	34 (16.3)	9 (11.8)	
		No	142 (67.9)	55 (72.4)	
	Breastfeeding period	12 months or less	21 (10)	11 (14.5)	0.0001
		12–24 months	174 (83.3)	39 (51.3)	

Qualitative variables		Control: frequency No. (%)	Case: frequency No. (%)	p-value
	over 24 months	14 (6.7)	26 (34.2)	

Table 3 indicates the univariate and adjusted association of independent variables with the Type 1 diabetes. The unadjusted results showed a significant association between Type 1 diabetes in children and the mothers without a history of diabetes (OR: 0.12, 95% CI: 0.01 to 0.12), maternal weight before pregnancy (OR: 0.94, 95% CI: 0.88 to 0.97), maternal overweight during pregnancy (OR: 0.84, 95% CI: 0.76 to 0.92), cesarean delivery (OR: 0.45, 95% CI: 0.25 to 0.81), Body Mass Index (BMI) of the mother being less than 18.5 (OR: 2.73, 95% CI: 1.28 to 5.79) before pregnancy, exclusive breastfeeding for more than six months [compared to less than 4 months] (OR: 0.42, 95% CI: 0.18 to 0.94) and the breastfeeding less than 12 months [compared to over 24 months) (OR: 3.54, 95% CI: 1.33 to 9.41).

Table 3
Unadjusted and adjusted odds ratio (OR) and 95% confidence interval (CI) of independent variables with the Type 1 diabetes in children aged 2 to 15 years

Quantitative-qualitative variables			Unadjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
Child's non-diet variables	Age		1.01 [0.94–1.09]	0.66	1.002[0.88–1.13]	0.97
	Fetal age at birth	More than 37 weeks [compared to less than 37 weeks]	0.77 [0.34–1.72]	0.53	1.43[0.27–7.59]	0.66
	Gender	Female [compared to male]	0.86 [0.50–1.47]	0.58	0.6[0.26–1.38]	0.23
	Birth weight	More than 2500 gr [compared to less than 2500 gr]	2.13 [0.37–2.14]	0.81	0.47[0.11–1.92]	0.29
	Weight at 1 year of age	More than 9500 gr [compared to less than 9500 gr]	1.25 [0.42–3.66]	0.68	1.21[0.04–3.62]	0.72
	Birth order	Third or fourth [compared to first or second]	0.72 [0.39–1.31]	0.28	0.5[0.2–1.23]	0.13
Mother's variables	Mother's age at delivery [years]		1.006[0.95–1.05]	0.81	1.02[0.94–1.14]	0.49
	History of diabetes	Gestational diabetes [compared to pre-gestational diabetes]	0.15[0.01–1.81]	0.13	0.04[0.001–1.15]	0.06
		No diabetes [compared to pre-gestational diabetes]	0.12 [0.01–0.12]	0.06	0.02[0.001–0.60]	0.02
	Mother's weight before pregnancy		0.94[0.88–0.97]	0.0001	0.88[0.84–0.91]	0.0001
	Mother's excess weight during pregnancy		0.84[0.76–0.92]	0.0001	0.83[0.75–0.93]	0.001

Quantitative-qualitative variables			Unadjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
	Method of delivery	C-section [compared to vaginal]	0.45[0.25–0.81]	0.007	0.56[0.24–1.3]	0.18
	Mother's BMI	Underweight [compared to normal)	2.73[1.28–5.79]	0.009	4.4[1.61–11.97]	0.004
		Overweight [compared to normal)	0.31 [0.14–0.70]	0.005	0.18[0.06–0.53]	0.002
		Obese [compared to normal]	0.20[0.02–1.59]	0.13	0.03[0.002–0.45]	0.011
	History of diabetes in first-degree family members	No [compared to Yes]	1.5[0.88–2.55]	0.13	1.76[0.79–3.87]	0.16
Child's diet and growth variables (in the first two years of life)	Exclusive breastfeeding	5 months [compared to less than 4 months]	0.17 [0.034–0.87]	0.03	0.08[0.006–1.06]	0.05
		6 months [compared to less than 4 months]	0.67[0.29–1.54]	0.35	0.35[0.07–1.68]	0.19
		More than 6 months [compared to less than 4 months]	0.42[0.18–094]	0.03	0.19[0.03–0.96]	0.04
	Status of the baby's weight gain chart during the first two years of life	Abnormal [compared to normal]	2.11[1.007–4.43]	0.049	6.98[2.16–22.5]	0.001
		Above the normal line [compared to below the normal line]	1.05[0.25–4.35]	0.94	1.31[0.19–8.93]	0.78
	Age of onset of complementary feeding	5 months [compared to less than 4 months]	0.87 [0.19–3.89]	0.86	15.25[0.88–262.01]	0.06

Quantitative-qualitative variables			Unadjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
		6 months [compared to less than 4 months]	0.72[0.20–2.59]	0.62	0.86[0.08–7.56]	0.86
		More than 6 months [compared to less than 4 months)	0.36[0.10–1.48]	0.17	0.54[0.05–5.65]	0.61
	Use of cow milk in the first year of life	No [compared to Yes]	0.56[0.26–1.21]	0.14	0.34[0.08–1.45]	0.14
	Use of artificial milk	Yes - along with breast milk [compared to No]	0.68[0.30–1.51]	0.35	0.54[0.24–0.1.32]	0. 30
		Yes -without breast milk [compared to No]	0.93[0.45–1.94]	0.86	1.38[0.45–4.24]	0.56
	Breastfeeding period	12–24 months [compared to over 24 months]	0.43[0.19–0.96]	0.04	0.89[0.17–4.62]	0.88
		Less than 12 months [compared to over 24 months)	3.54[1.33–9.41]	0.01	10.52[1.62–66.64]	0.01

Finally, the results of multiple backward logistic regression showed that Body Mass Index (BMI) of the mother being less than 18.5 before pregnancy (OR: 4.4, 95% CI: 1.61 to 11.97), mothers without a history of diabetes (OR: 0.02, 95% CI: 0.001 to 0.60), mother's weight before pregnancy (OR: 0.88, 95% CI: 0.84 to 0.91), mother's excess weight during pregnancy(OR: 0.83, 95% CI: 0.75 to 0.93), exclusive breastfeeding for more than six months (OR: 0.19, 95% CI: 0.03 to 0.96), low weight gain in the first two years of life (OR: 6.98, 95% CI: 2.16 to 22.5), and the breastfeeding less than 12 months (OR: 10.52, 95% CI: 1.62 to 66.64) have association with Type 1 diabetes ($p < 0.05$) (Table 3).

Discussion

The results of this study showed that exclusive breastfeeding for six months and more can be effective in preventing the development of T1DM in children (OR = 0.19). While several other studies have also

reported that exclusive breastfeeding can prevent T1DM (17, 21–24), there are also reports to the contrary (25).

Over the last three decades, the prevalence of obesity has more than doubled in children and tripled in adolescents (26). Short-term breastfeeding and early introduction of complementary foods may be associated with respiratory and gastrointestinal infections and obesity in children (14). Also, the consumption of excess protein in childhood is associated with an increase in BMI at older ages. The protein contained in artificial milk can also lead to the secretion of insulin and insulin-like growth factor, which may explain why formula-fed babies have higher plasma insulin levels than breastfed children (21). The results of this study showed higher odds of developing T1DM in children whose weight gain was below the normal growth line (OR: 6.98) and also those whose weight gain was above the normal growth line (OR: 1.31). It was also found that exclusively breastfed babies had lower odds of developing T1DM at an older age than exclusively formula-fed ones (OR: 0.19). This suggests that exclusive formula feeding is associated with a higher risk of T1DM, and is consistent with the findings of Rabiei et al. (21), which showed a higher risk of T1DM at an older age in babies breastfed for less than 12 months compared to those breastfed for more than 24 months (OR: 10.52).

This study found no association between T1DM and cow milk consumption in the first year of life, which is consistent with the results of Rabiei et al. (21) and Savilahti & Saarinen (27). It appears that the early introduction of complementary foods may also stimulate the development of T1DM by disrupting the autoimmune responses. This is especially true for children who are genetically predisposed to diabetes (27, 28).

In this study, children whose complementary feeding had started before the age of fourth months were 46% more likely to develop T1DM than those whose complementary feeding had started after the age of six months. However, this relationship was not statistically significant.

The results show that mother’s excess weight during pregnancy decreases the odds of the development of T1DM in the baby. Rasmussen et al in a study showed that, having less than 10.75kg excess weight during pregnancy decreases the risk of T1DM in the child by approximately 17%(29).

As of this writing, only a handful of studies have investigated the effect of having diabetes before or during pregnancy (gestational or pregestational) on the risk of diabetes in the delivered child, and it is still not clear whether the breast milk of diabetic mothers has the same ingredients as the breast milk of healthy mothers. Some researchers believe that breastfeeding from diabetic mothers is also effective in preventing diabetes in children (17, 22). However, others have suggested that the breast milk of diabetic mothers should be considered a risk factor for the development of diabetes in children (21). In the present study, the incidence of T1DM in children had a direct relationship with the mothers having diabetes during pregnancy (gestational diabetes), but had no relationship with diabetes in the child’s other first-degree family members, which is consistent with other reports (21, 29).

Breastfeeding has nutritional, immunological, and physiological benefits. It also plays an important role in the formation of a healthy maternal attachment and the healthy development of the baby (30). Some researchers believe that the method of delivery affects the success of breastfeeding, as mothers who give birth naturally tend to breastfeed their baby for longer than those who give birth by C-section (30, 31). In the present study, there was no significant difference in terms of incidence of T1DM between the children born vaginally and those born by C-section. Therefore, there seems to be no relationship between the incidence of diabetes and the type of delivery. While this conclusion is consistent with the findings of Rabiei et al. (21), it should be noted that not many studies have been conducted on this relationship.

One of the limitations of this study was that some respondents in both case and control groups had difficulty recalling the information of interest. This problem had two dimensions. The first was the general differences among the respondents in terms of their capacity to recall events. To resolve the issue, researchers tried to compare the respondents' inputs with their medical records and detect and correct inconsistencies as much as possible. The second dimension was the difference (bias) between the mothers in the case group and those in the control group in terms of accuracy in remembering the event related to their child. This is because mothers in the case group often wonder why their children has this condition and whether they have done something wrong that has contributed to their child becoming diabetic. Therefore, these mothers are often more accurate in recalling past events and information related to their child, and this creates a bias, which is one of the inherent problems of case-control studies.

Conclusion

Body mass index less than 18 mothers before pregnancy, Low weight gain in the first two years of life and breastfeeding less than 12 months increases the risk of developing Type-1 Diabetes in children. However, the findings did not confirm the role of the early introduction of complementary food and the use of cow milk in the development of T1DM. Considering the findings of this study and the proven health benefits of breastfeeding, it is recommended to commit to exclusive breastfeeding for at least six months after birth.

Abbreviations

T1DM
Type 1 Diabetes Mellitus
IGT
Impaired Glucose Tolerance

Declarations

Ethics approval and consent to participate

The ethics committee of Jahrom University of Medical Sciences (Code: IR.JUMS.REC.2017.173) approved this study. All participant gave written consent to take part in the study.

Consent to publish

Not applicable.

Availability of data and materials

The data are available from the corresponding authors.

Competing interests

The authors declare that they have no conflict of interests.

Funding

The Jahrom University of Medical Sciences funded the study.

Authors' Contributions

The idea of this study was initiated by MZ. MZ and AN and VR contributed to design, management of the study and writing of the manuscript. SA contributed to data collection. VR participated in performed the statistical analysis and writing of the manuscript. HK contributed in writing of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Hereby, the authors extend their gratitude to the research deputy of Jahrom University of Medical Sciences for their support and confirmation of the project. In addition, thanks are owed to the participants for their cooperation in this study.

References

1. Baden MY, Imagawa A, Abiru N, Awata T, Ikegami H, Uchigata Y, et al. Characteristics and clinical course of type 1 diabetes mellitus related to anti-programmed cell death-1 therapy. Diabetol Int. 2019;10(1):58-66.
2. Rak K, Bronkowska M. Immunomodulatory Effect of Vitamin D and Its Potential Role in the Prevention and Treatment of Type 1 Diabetes Mellitus-A Narrative Review. Molecules. 2018;24(1):50.
3. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. Lancet. 2018;391(10138):2449-62.
4. Rogers MA, Kim C, Banerjee T, Lee JM. Fluctuations in the incidence of type 1 diabetes in the United States from 2001 to 2015: a longitudinal study. BMC medicine. 2017;15(1):199.

5. Vaiserman A, Carstensen B, Voitenko V, Tronko M, Kravchenko V, Khalangot M, et al. Seasonality of birth in children and young adults (0–29 years) with type 1 diabetes in Ukraine. Diabetologia. 2007;50(1):32-5.
6. Krzewska A, Ben-Skowronek I. Effect of Associated Autoimmune Diseases on Type 1 Diabetes Mellitus Incidence and Metabolic Control in Children and Adolescents. Biomed Res Int. 2016;2016:6219730.
7. Soltesz G, Patterson C, Dahlquist G, Group ES. Worldwide childhood type 1 diabetes incidence–what can we learn from epidemiology? Pediatric diabetes. 2007;8:6-14.
8. Jarosz-Chobot P, Polanska J, Szadkowska A, Kretowski A, Bandurska-Stankiewicz E, Ciechanowska M, et al. Rapid increase in the incidence of type 1 diabetes in Polish children from 1989 to 2004, and predictions for 2010 to 2025. Diabetologia. 2011;54(3):508-15.
9. Green A, Patterson CC, Group ETS. Trends in the incidence of childhood-onset diabetes in Europe 1989–1998. Diabetologia. 2001;44(3):B3-B8.
10. Erkkola M, Pigg H-M, Virta-Autio P, Hekkala A, Hyppönen E, Knip M, et al. Infant feeding patterns in the Finnish type I diabetes prediction and prevention nutrition study cohort. European journal of clinical nutrition. 2005;59(1):107-13.
11. Rahmanian V, Sarikhani Y, Rahmanian K, Mansoorian E, Zare M. Factors associated with failure to thrive among children aged 3 to 72 months in Jahrom, southern Iran. Shiraz E Medical Journal. 2018;19(4).
12. Strotmeyer ES, Yang Z, LaPorte RE, Chang Y-F, Steenkiste AR, Pietropaolo M, et al. Infant diet and type 1 diabetes in China. Diabetes research and clinical practice. 2004;65(3):283-92.
13. Patelarou E, Girvalaki C, Brokalaki H, Patelarou A, Androulaki Z, Vardavas C. Current evidence on the associations of breastfeeding, infant formula, and cow's milk introduction with type 1 diabetes mellitus: a systematic review. Nutrition reviews. 2012;70(9):509-19.
14. Nucci AM, Virtanen SM, Sorkio S, Bärlund S, Cuthbertson D, Uusitalo U, et al. Regional differences in milk and complementary feeding patterns in infants participating in an international nutritional type 1 diabetes prevention trial. Maternal & child nutrition. 2017;13(3):e12354.
15. Chmiel R, Beyerlein A, Knopff A, Hummel S, Ziegler A-G, Winkler C. Early infant feeding and risk of developing islet autoimmunity and type 1 diabetes. Acta diabetologica. 2015;52(3):621-4.
16. Sorkio S, Cuthbertson D, Bärlund S, Reunanen A, Nucci AM, Berseth CL, et al. Breastfeeding patterns of mothers with type 1 diabetes: results from an infant feeding trial. Diabetes Metab Res Rev. 2010;26(3):206-11.
17. Malcova H, Sumnik Z, Drevinek P, Venhacova J, Lebl J, Cinek O. Absence of breast-feeding is associated with the risk of type 1 diabetes: a case-control study in a population with rapidly increasing incidence. Eur J Pediatr. 2006;165(2):114-9.
18. Kähm K, Laxy M, Schneider U, Rogowski WH, Lhachimi SK, Holle R. Health Care Costs Associated With Incident Complications in Patients With Type 2 Diabetes in Germany. Diabetes Care. 2018;41(5):971-8.

19. Huber CA, Schwenkglenks M, Rapold R, Reich O. Epidemiology and costs of diabetes mellitus in Switzerland: an analysis of health care claims data, 2006 and 2011. BMC Endocr Disord. 2014;14:44.
20. Golkari A, Moeini A, Jabarifar SE. Relationship Of Socioeconomic Status With Quality Of Life Related To Oral And Dental Health Of 2?5-Year-Olds In Shiraz Journal Of Isfahan Dental School. 2014;9(6):534-41.
21. Rabiei S. The association of nutrition style through the first 2 years of life with type 1 diabetes mellitus and some of the other effective factors in 2-15 years old children. Iranian Journal of Endocrinology and Metabolism. 2011;13(1):9-17.
22. Gunderson EP. Breast-feeding and diabetes: long-term impact on mothers and their infants. Current diabetes reports. 2008;8(4):279-86.
23. Rosenbauer J, Herzig P, Giani G. Early infant feeding and risk of type 1 diabetes mellitus—a nationwide population-based case–control study in pre-school children. Diabetes/metabolism research and reviews. 2008;24(3):211-22.
24. Stuebe A. The risks of not breastfeeding for mothers and infants. Reviews in obstetrics and gynecology. 2009;2(4):222.
25. Samuelsson U, Johansson C, Ludvigsson J. Breast-feeding seems to play a marginal role in the prevention of insulin-dependent diabetes mellitus. Diabetes research and clinical practice. 1993;19(3):203-10.
26. Sanyaolu A, Okorie C, Qi X, Locke J, Rehman S. Childhood and Adolescent Obesity in the United States: A Public Health Concern. Glob Pediatr Health. 2019;6:2333794X19891305.
27. Savilahti E, Saarinen KM. Early infant feeding and type 1 diabetes. Eur J Nutr. 2009;48(4):243-9.
28. Luopajärvi K, Savilahti E, Virtanen SM, Ilonen J, Knip M, Åkerblom HK, et al. Enhanced levels of cow's milk antibodies in infancy in children who develop type 1 diabetes later in childhood. Pediatric diabetes. 2008;9(5):434-41.
29. Turtinen M, Härkönen T, Parkkola A, Ilonen J, Knip M. Characteristics of familial type 1 diabetes: effects of the relationship to the affected family member on phenotype and genotype at diagnosis. Diabetologia. 2019;62(11):2025-39.
30. Cetisli NE, Arkan G, Top ED. Maternal attachment and breastfeeding behaviors according to type of delivery in the immediate postpartum period. Rev Assoc Med Bras (1992). 2018;64(2):164-9.
31. Örün E, Yalçin SS, Madendag Y, Üstünyurt-Eras Z, Kutluk S, Yurdakök K. Factors associated with breastfeeding initiation time in a Baby-Friendly Hospital. The Turkish journal of pediatrics. 2010;52(1):10-16.