



## Comparison of Type I Diabetes Frequency in Children with Cesarean and Normal Vaginal Delivery

Sezaryen ve Normal Vajinal Doğan Çocuklarda Tip 1 Diyabet Sıklığının Karşılaştırılması


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### ABSTRACT

**Aim:** The effect of type 1 diabetes mellitus over the world is rising day after day. There are controversial results that may be related to cesarean delivery that has become widespread in recent years and the risk of type 1 diabetes mellitus. In this study, we aimed to investigate the frequency of type 1 diabetes mellitus in children born by cesarean delivery or normal vaginal delivery, considering that there may be an association between mode of birth way and diabetes mellitus.

**Material and Methods:** The study was organized with 368 children who were diagnosed as type 1 diabetes mellitus between 8-16 ages that applied to the diabetes outpatient clinic in 2019. The patients were grouped according to the mode of delivery. Descriptive data such as age, gender, HBA1c, and BMI were evaluated retrospectively.

**Results:** The children with type 1 diabetes mellitus, cesarean delivery show 33.2% more than normal vaginal delivery ( $p<0.001$ ). While 9.0% of children with cesarean delivery had mother's diabetes mellitus, this rate was 5.7% in children with normal vaginal delivery. Similarly, 5.3% of children with cesarean delivery had diabetes mellitus in their father, while this rate was 8.9% in children with normal vaginal delivery.

**Conclusion:** According to the results of this study, cesarean delivery may have a significant effect on the risk for type 1 diabetes mellitus in childhood either adolescence. Even if parents with diabetes were not included, it was found that cesarean delivery have meaningful relation by diabetes mellitus stimulation. Regarding this, further studies are needed.

**Keywords:** Cesarean delivery; normal vaginal delivery; type 1 diabetes.

### ÖZ

**Amaç:** Tip 1 diyabetin dünya üzerindeki etkisi her geçen gün artmaktadır. Son yıllarda yaygınlaşan sezaryen doğum ve tip 1 diyabet riski arasında ilişkili olabilecek tartışmalı sonuçlar vardır. Bu çalışmada, doğum şekli ve tip 1 diyabet arasında bir bağlantı var olduğunu düşünerek sezaryen ve normal vajinal yolla doğan çocuklarda tip 1 diyabet görülme sıklığının araştırılması amaçlandı.

**Gereç ve Yöntemler:** Araştırmaya 2019 yılında diyabet polikliniğine başvuran 8-16 yaşları arasında olan tip 1 diyabet tanısı konmuş 368 çocuk dahil edildi. Hastalar doğum şekline göre gruplandırıldı. Hastalardan elde edilen yaş, cinsiyet, HBA1c ve BMI gibi tanımlayıcı veriler geriye dönük olarak değerlendirildi.

**Bulgular:** Tip 1 diyabet tanısı olan çocuklarda sezaryen doğumun normal vajinal doğuma göre %33,2 daha fazla olduğu görüldü ( $p<0,001$ ). Sezaryen ile doğan çocukların %9,0'unun annesinde diyabet tanısı bulunurken, normal vajinal yolla doğan çocuklarda bu oran %5,7 idi. Benzer şekilde, sezaryen ile doğan çocukların %5,3'ünün babasında diyabet tanısı bulunurken, normal vajinal yolla doğan çocuklarda bu oran %8,9 idi.

**Sonuç:** Bu çalışmadan elde edilen sonuçlara göre, sezaryen doğum çocukluk veya ergenlik döneminde tip 1 diyabet riski üzerinde önemli bir etkiye sahip olabilir. Bununla birlikte, diyabetli ebeveyn olguları dahil edilmese bile, sezaryen ile doğum ve tip 1 diyabet arasında önemli bir ilişki olduğu bulunmuştur. Bununla ilgili olarak, daha ileri çalışmalara ihtiyaç duyulmaktadır.

**Anahtar kelimeler:** Sezaryen doğum; normal vajinal doğum; tip 1 diyabet.

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## INTRODUCTION

Diabetes mellitus (DM) is one of important metabolic diseases defined as hyperglycemia caused by secretion or activity of impaired insulin (1). Some patients with diabetes might life-threatening experience as acute hyperglycemic attacks, while others may life-threatening experience as acute hypoglycemic attacks for outcome diabetes treatment (2). During disease progression, some complications such as retinopathy, nephropathy, neuropathy, atherosclerosis and gangrene might be seen (3). Diabetes is a common disease whose true prevalence is unknown and the population of patients have diabetes are increasing day by day. While the estimated number of patients were around 380 million in 2014, this number is expected to reach 592 million by 2035 (4). In the national health and nutrition analysis conducted using fasting blood sugar and oral glucose tolerance test at 2005/2006, and it was determined that the prevalence of diabetes was 12.9% in individuals under 20 years of age in the United States. This rate of 12.9% corresponds to approximately 40 million people (5). In a study on pre-diabetes prevalence in adults with diabetes in 2010 in China (6), diabetes was 11.6% (effected 113.9 million people), and pre-diabetes was 50.1% (effected 493.4 million people). For classification made in 1979, two main kinds of diabetes were identified: type 1 (insulin dependent, IDDM) and type 2 (non insulin dependent, NIDDM). Among cases of total diabetes, 5-10% patients with DM are in the type 1 group approximately (7).

Patients often have a sudden onset such as polyuria and rapid weight loss. Patients have insulin deficiency as a result of a problem caused by pancreatic beta cells. The peak incidence occurs in childhood and adolescence. Type 2 group accounts for 90% of all patients with DM (8). The symptoms in patients are minimal and not prone to ketosis. In this group of patients, insulin concentrations may be normal, decreased or increased. In this form of diabetes, the effect of insulin is generally impaired. It is commonly associated with obesity and weight loss alone can control hyperglycemia. However, many individuals with type 2 diabetes may need dietary intervention, antihypertensive agents, or insulin therapy to control hyperglycemia (9). Although the disease can be seen at a young age, it usually occurs after the age of 40 (8).

Worldwide cesarean delivery is increasing day by day. Scientific progress, social, cultural and legal changes have led to a fundamental cesarean change between patients and doctors (10). Changing risk profiles and previous cesarean births in old primiparas may contribute to the increase of the number of cesarean people (11). Despite all these perspectives, cesarean birth has numerous potential complications (infection, organ injuries, blood transfusion need) for mother and baby (12). Apart from the risks during the operation, there are many postpartum complications such as thromboembolism (10). There are various risks (such as uterine rupture, placenta previa) in women who have delivered by cesarean (13). In recent years, it has been observed that there may be some risks (neonatal respiratory distress, allergic rhinitis, pulmonary hypertension, type 1 DM) in babies born by cesarean section (14-16).

In 1991, 15.3% of all births in Germany were performed by cesarean, while in 2012 this rate was 31.7% (17). The

cesarean rate in Sub-Saharan Africa is 3%, 31% in Central America and 32.2% in the USA (18,19). This elevation can be explained by a rising tendency to avoid risk, obstetric practice adaptation and increased media caution. It was carried out in the European Union in 2000 with 221 cesarean per 1000 live births, this rate increased to 268 per 1000 live births in 2011 (17).

Many studies have investigated cesarean section regarding the threatening of type 1 diabetes in childhood. A meta-analysis results involved 16 observational studies showed that there is a potential relationship among higher frequency of cesarean section and an increased risk of type 1 DM (20). In the meta-analysis included 20 retrospective studies, there was a 20% increase at childhood-onset type 1 diabetes risky in children giving birth by cesarean section (21). Many studies have researched cesarean and type 1 diabetes, however in some studies, the findings have been incoherent, possibly as a cause of insufficient sampling and limited strength. The aim of this study is to determinate whether a relationship with the risk of type 1 diabetes in children born with cesarean section and normal vaginal delivery.

## MATERIAL AND METHODS

The literature review was done using PubMed and using the keywords "cesarean delivery", "normal vaginal delivery", "mode of delivery", "diabetes mellitus, type 1", "IDDM". The researches carried out mostly belonged to 2007 and before. The data in the patient files of all children who were between 6-18 ages who applied to the Endocrinology outpatient clinic of Düzce University in 2019, were diagnosed with type 1 DM, and their HbA1c value was above 6%, were analyzed retrospectively. Children who have type 1 DM between the ages of 8 and 16, having a mode of delivery in epicrisis, maternal body mass index (BMI) 20-30 and children with elective cesarean section and normal vaginal delivery were included in the study. The criteria for exclusion are children under the age of 8 and over 16, lack of natal knowledge in epicrisis, children with urgent cesarean delivery and the mother has any chronic conditions. According to the information obtained from the patient files, the patients were separated with two groups as normal vaginal birth and elective cesarean birth. 368 of 1574 patients who contain the inclusion criteria were included in the study. Of the 368 patients, 205 (55.7%) were male and 163 (44.3%) were female. This study was approved by Düzce University Non-Interventional Health Research Ethics Committee (02.03.2020 and 2020/29) prior to any data collection. In accordance with the Helsinki Declaration Principles, "informed consent" was taken from the patients who participated in the study.

### Statistical Analysis

Descriptive statistics for categorical variables were used as numbers and percentages, and mean and standard deviation (SD) for numerical variables. Pearson chi-square test was used to examine between type of birth and the proportion of children with type 1 DM as well as obstetric features such as the number of parents with diabetes or non-diabetes and sex of the child. Kolmogorov-Smirnov tests were used to determine the suitability of variables for normal distribution. For univariate analyzes between

cesarean section and normal vaginal birth groups, Student's t-test was used. SPSS 20.0 software was used for statistical analysis, and p values <0.05 were regarded as statistically significant.

## RESULTS

Amongst 368 children with birth way data, 245 were born by cesarean delivery and 123 by normal vaginal delivery. The most cases (66.6%) of children with type 1 DM were born by cesarean section. Besides that, 33.4% of children with type 1 DM were born by normal vaginal delivery. The children who have type 1 DM, cesarean section births show 33.2% more than normal vaginal delivery ( $p < 0.001$ ). There was no statistically significant difference in gender, maternal age and BMI of children with diabetes between cesarean delivery and normal vaginal delivery groups; thus, homogeneity between the groups is provided.

The number of mothers and fathers with diabetes are shown in Table 1. The number of mothers with diabetes in cesarean birth group ( $n=22$ , 9.0%) is higher compare to normal vaginal birth group ( $n=7$ , 5.7%). However, the number of fathers with diabetes in normal vaginal birth group ( $n=11$ , 8.9%) is higher than in cesarean birth group ( $n=13$ , 5.3%). When it is evaluated separately according to the type of birth and the diabetes status of the parents, children with type 1 diabetes, whose parents non-diabetes, were common in the cesarean section delivery group ( $n=210$ , 85.7%) according as vaginal normal delivery group ( $n=105$ , 85.4%).

## DISCUSSION

We evaluated all children between the ages of 6 and 18 who were admitted to the pediatric type 1 DM outpatient clinic in 2019 year which diagnosis of type 1 diabetes using hospital automation throughput. In accordance with results, the frequency of type 1 diabetes was significantly higher for children born with cesarean birth compared to children born with vaginal birth way. Samuelsson et al. (22) found an increased risk of type 1 DM for children born by cesarean in a study in Norway. However, there was no increased risk for children of non-diabetic mothers, whereas there was an increased risk for cesarean delivery in children born from diabetic mothers. They attribute that increased risk of diabetic mothers to diabetic mothers giving birth more frequently by cesarean. From our

retrospective study, we found that the ascending population of type 1 diabetes in children born by cesarean section continues when we exclude children with DM in their family (mother or father).

The increase of the risk of type 1 DM in children born with cesarean was observed in almost all studies conducted in this direction. However, other factors that cause diabetes type 1 in childhood (gestational age, birth weight, maternal age, breastfeeding and maternal diabetes) cause complexity to clarify relationship cesarean delivery and type 1 diabetes.

In a meta-analysis study conducted in 2010, type 1 diabetes was %10 risk increasement observed in children born with a birth weight over 4 kg compared to those born with 3-3.5 kg (23). The findings of the more population study holded by Khashan et al. (24) were consistent with synchronization results of this study. Another study published in 2014, the risk of occurs type 1 diabetes in childhood was found to be 18% in preterm infants (25). Additionally, Bingley et al. (26) found a strong relationship between high maternal age and an increased risk of developing diabetes in the child.

Cardwell et al. (15,23) found that high birth weight, short gestation period and high maternal age increased the risk of diabetes at child in a meta-analysis conducted over twenty studies. Moreover, when other risk factors (gestational age, birth weight, maternal age, breastfeeding of the baby and maternal diabetes) that were stated to exist for type 1 diabetes were added, a very small augmentation for risk of cesarean delivery was observed. On the other hand, without these factors, cesarean under elective conditions increased the risk of type 1 diabetes by approximately 20%. Compatible with Cardwell et al. research, when the presence of type 1 diabetes was excluded in the mother or father, we also found that the rate of cesarean delivery among children with type 1 diabetes was significantly higher than the normal vaginal delivery.

Many patients with type 1 diabetes have autoimmune damage mediated by T cells of pancreatic beta cells, some are idiopathic (27-29). Islet cell cytoplasmic antibodies (30), insulin autoantibodies (31), antibodies to glutamic acid decarboxylase (32), insulinoma-associated antigens (33), zinc transporter ZnT8 (34) are the best-defined autoantibodies associated with type 1 diabetes.

Although some hypothesis (intestinal microbiota, bacterial revelation during pregnancy, perinatal period stress and hygiene) have been suggested in increasing the risk of type 1 diabetes with cesarean delivery, it is not fully understood what the possible offender is. However, the most prominent of these hypotheses is the altered intestinal microbiota. It is thought that intestinal microbiota plays an important drive to stimulate the progress of immune system (35).

Novel studies have indicated that the intestinal microbiota of a child born by cesarean or normal vaginal birth is different (36). In a prospective study, the rate of bifidobacterium and lactobacillus-like bacterial colonization delayed in the cesarean babies of the mother who had antibiotic prophylaxis, and the rate of babies who gave birth in a normal vaginal way in 1 month and 10 days. This study also showed that changes on intestinal flora of a baby born by cesarean would not take less than 6 months (37).

**Table 1.** Demographic and obstetric characteristics

	Elective Cesarean Delivery (n=245)	Normal Vaginal Delivery (n=123)	P
Maternal age	29.50±4.15	29.3±1.07	0.599
Maternal BMI	24.21±3.77	23.68±1.94	0.144
HbA1c	8.52±2.15	8.14±1.86	0.096
Gender			
Male	102 (41.6%)	61 (49.6%)	0.147
Female	143 (58.4%)	62 (50.4%)	
Parents with DM			
Mother	22 (9.0%)	7 (5.7%)	0.248
Father	13 (5.3%)	11 (8.9%)	
None	210 (85.7%)	105 (85.4%)	

BMI: Body mass index, HbA1c: Hemoglobin A1c, DM: Diabetes Mellitus

Beside those in vivo experiments, normal intestinal flora has been shown to have an immunostimulating effect. Mucosal sort IgA cells are relatively less than immune-suppressed animals (38). The fact that babies born with cesarean are relegated high risk of improving type 1 diabetes in childhood compared to children born with a normal vaginal route may be a late-activated immune system due to the difference in intestinal microbiota in these children, or another reason might be investigated (39). Further studies are needed to make etiopathogenic mechanism more clear about the frequency of diabetes and the way of birth.

**Conflicts of Interest:** The authors declared that no conflicts of interest.

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