

# Birth Weight and Childhood Onset Type 1 Diabetes: A Case-Control Study in Shiraz, South of Iran

Z. Karamizadeh, H. Jalaeian,  
M.A. Kashef, M. Ebrahimi

## Abstract

To determine the relation between birth weight and age of presentation of type 1 diabetes and assess its risk factors, a case-control study was done on all diabetic patients under the age of 15, who were registered in Shiraz Diabetic Center or admitted in Namazi Hospital. A case group of 87 diabetic patients were matched with a control group of 100 healthy individuals. Birth weight  $\geq 4$ kg was determined to be a risk factor for diabetes (odds ratio: 2.04). A weak association was found between birth weight  $\leq 2.4$  kg and diabetes development.

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**Keywords** • Birth weight • diabetes mellitus type 1 • risk factors

## Introduction

**T**ype 1 diabetes is caused by immune mediated destruction of the pancreatic  $\beta$  cells. Both genetic and non-genetic factors are involved in its pathogenesis, but factors which initiate the destructive processes of pancreatic  $\beta$  cells are not fully identified.<sup>1,2,3</sup> Type 1 diabetes is usually characterized by its abrupt clinical onset. There is evidence that even in young children, the destructive processes precede the clinical presentation for years.<sup>3</sup> It is possible that environmental exposure eventually leading to type 1 diabetes may have occurred during infancy or in uterus.<sup>2,3</sup>

There is controversy in literature about the risk factors associated with type 1 diabetes in prenatal and early neonatal life. Some surveys pointed out that high birth weight may act as a risk factor.<sup>2,4</sup> Others believe the opposite is true,<sup>5</sup> however, most reports do not reveal a strong association.<sup>6</sup>

Some other associations are often suggested, but not agreed upon. They include maternal age, not being breastfed, having been exposed to cow milk in early life, consumption of smoked food by the mother at the time of conception, mother's smoking, caesarean section, maternal enteroviral infection, the average weight gain during infancy, preeclampsia, maternal-child blood group incompatibility, age of introduction of supplementary milk-feeding and solid foods, first-born children, etc.<sup>1,3,7,8</sup>

## Subjects and Methods

This is a case-control study on birth weight and age of clinical onset of type 1 diabetes. Records of all diabetic patients less than 15-year old, admitted during a four-year period in the pediatric endocrinology ward of Shiraz Namazi hospital, and were reviewed. Also we studied the records of all diabetic patients  $\leq 15$  yr who were registered in Shiraz diabetic center. Children

Department of Pediatrics,  
Namazi Hospital,  
Shiraz University of Medical Sciences,  
Shiraz, Iran.

### Correspondence:

Zohreh Karamizadeh MD,  
Division of Pediatric Endocrinology,  
Department of Pediatrics,  
Namazi Hospital,  
Shiraz University of Medical Sciences,  
Shiraz, Iran.  
**Tel/Fax:** +98 711 6265024  
**E-mail:** [jalah@sums.ac.ir](mailto:jalah@sums.ac.ir)

with cystic fibrosis, major congenital anomalies, or those who were parts of twin or higher order of deliveries were excluded from the study.

A total of 100 healthy children were designed as control group. Patient/Control subject differences in the mean of the birth weight were calculated. Statistical analyses were performed using Mann-Whitney and Students *t* tests with  $P < 0.05$ .

## Results

Demographic data of case and control groups is presented in Table 1. Eighty-seven diabetic patients (46 boys and 41 girls) compared with 100 healthy individuals (54 boys and 46 girls). There was no statistical significant difference in the mean age and sex ratios. Table 2 depicts distribution of case and control participants in different birth weight intervals. For birth weights  $\geq 4$  kg, odds ratio (OR), was equal to 2.04. In addition, there was a weak association between birth weight  $\leq 2.4$  kg and diabetes development. (OR: 1.47)

**Table 1:** Demographic data of diabetic children (case; n=87) and healthy individuals (control; CNT, n=100)

	Case n (%)	CNT n (%)
Age (yr)	9.1±5.2	8.9±4.9
Male (%)	46 (53)	54 (54)
Female (%)	41 (47)	46 (46)

**Table 2:** Odds ratio (OR) of birth weight (BW) for development of diabetes in children (case) in relation to healthy participants (control, CNT)\*

Weight (kg)	Case n (%)	CNT n (%)	OR	95% CI
$\leq 2.4$	6 (7)	5 (5)	1.47	0.4-5.2
2.5-2.95	19 (22)	24 (24)	0.97	0.5-2.0
3-3.45	40 (46)	49 (49)	1.00	Baseline
3.5-3.95	17 (19)	19 (19)	1.10	0.5-2.4
$\geq 4$	5 (6)	3 (3)	2.04	0.5-9.1
Total	87	100		

Mantel-Haenszel common OR estimates

The mean birth weight of diabetic patients ( $3.20 \pm 0.53$ kg) and healthy participants ( $3.13 \pm 0.47$ kg) was not significantly different. The mean age of onset of type 1 diabetes was  $7.17 \pm 3.23$  yrs (range; 1.5-15 years). The age of onset of diabetes in patients with birth weights  $\leq 2.5$  Kg was  $3.41 \pm 1.46$  years which is considerably lower than the age of clinical presentation of cases with birth weight  $\geq 4$ kg ( $7.44 \pm 3.15$  years;  $P < 0.002$ ).

## Discussion

Age of onset of diabetes is higher in high birth weight groups. Patients with birth weights  $\geq$  four kg have later onset of diabetes compared to those with birth weights 2.5-4 kg. Also 2.5-4 kg

cases have a later onset compared to individuals with birth weights  $< 2.5$ kg. Therefore, as the most significant finding in this study, we have found a linear relationship between the mean age of onset of diabetes and birth weight.

Although no significant difference was observed between birth weights of diabetic and non-diabetic children, we found OR of 2.04 for the development of diabetes in high birth weight diabetic patients. This observation is in agreement with other studies considering the increase in birth weight as a risk factor for the development of insulin dependent diabetes mellitus.<sup>2,6,9-11</sup>

There are some explanations in the literature for the role of high birth weight in diabetes type 1. For instance, some genetic factors may predispose to both higher birth weight and type I diabetes.<sup>2</sup> There are also some biological mechanisms. Insulin is said to be the most important growth factor during the late pregnancy.<sup>2,12</sup> Actively pancreatic  $\beta$  cells that are secreting insulin at this stage are more prone to immune-mediated destruction than those of less active ones. Therefore, augmented activity of  $\beta$  cells in high birth weight individuals makes them more susceptible to diabetes development.<sup>2,13</sup>

To summarize, in our population, birth weight seems to be an important risk factor for development of childhood or early adolescence diabetes.

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