

# Risk of Overweight in Adolescence among Offspring of Diabetic Mothers

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The incidence of diabetes mellitus (DM) is rising continuously worldwide. It is known that diabetes during pregnancy has both short- and long-term adverse effects for the offspring. Data on the long-term effects in young adulthood are scant.

Two studies, one from Denmark [1] and another from Israel [2], about offspring born to diabetic mothers were conducted in military conscripts. The authors found that offspring of diabetic mothers (ODM) were almost 6 kg heavier than the control group [1] and had a higher mean body mass index (BMI) and blood pressure [2]. However, the first study was limited to males (women are not drafted to military service in Denmark), and the second study evaluated subjects born more than 40 years ago.

The aims of the present study were to investigate the effects of maternal diabetes during pregnancy on anthropometric measures of ODM at birth and at age 17 years.

## PATIENTS AND METHODS

The electronic database at the Schneider Children's Medical Center of Israel, was searched for all full-term singleton neonates born to a mother with diabetes between 1987 and 1993. For each neonate in the ODM group, we identified the next full-term singleton neonate in the department who was born to a mother without diabetes.

All infants included in the study were traced to age 17 years by matching their identification number to the computerized database of the Israel Defense Forces.

The study was approved by the institutional review boards of the Rabin Medical Center and the Israel Defense Forces Medical Corps. Subject anonymity was strictly maintained.

\*The first and second authors contributed equally to this study

## RESULTS

A total of 544 neonates were born to mothers with DM during the study period: 102 neonates were excluded (61 pre-term, 13 post-term, 28 twins). Thus, the original cohort consisted of 442 ODM and a matching number of controls.

Data at age 17 years were available for 666 subjects (75.3% of the original cohort): 329 in the ODM group (193 boys and 136 girls) and 337 in the control group (193 boys and 144 girls).

A higher percentage of the ODM group was born at birth weight above the 90th percentile (males: 22.8% vs. 8.3%,  $P < 0.001$ ; females: 14% vs. 4.9%,  $P = 0.003$ ) and at birth length above the 90th percentile (11.4% vs. 3.6%,  $P = 0.003$ ).

At age 17 years, mean weight was higher in the ODM group than the control group, by 2.6 kg for males ( $P = 0.05$ ) and by 2.7 kg for females ( $P = 0.06$ ). Being overweight (BMI > 85th percentile) was significantly more prevalent among males in the ODM group than in the control group (26.9% vs. 16.1%,  $P = 0.006$ ). There were no between-group differences in mean height for either gender.

On multivariable analysis including birth weight and ODM, maternal diabetes during pregnancy and birth weight above 90th percentile had a conjoint effect on the risk of being overweight at age 17 years. Odds ratio for ODM and birth weight above 90th percentile was 2.82, confidence interval 1.56–5.10,  $P < 0.001$ , compared to controls [Table 1].

## DISCUSSION

We found that diabetes during pregnancy is associated with increased risk to birth weight and length above the 90th percentile. These findings compare well with previous data on ODM worldwide [3]. The increase in birth measurements of ODM is attributed to maternal hyperglycemia. Glucose is transferred via the placenta and induces hyperinsulinemia in the fetus, which in turn leads to increased fetal fat tissue and stimulates linear growth [4].

Earlier studies have shown that diabetes during pregnancy is associated with being overweight in childhood [5]. Our

**Table 1.** Anthropometric measures of offspring of diabetic mothers and non-diabetic mothers at birth and at age 17 years, by gender

Variable	Male			Female		
	ODM N=193	Control N=193	P value	ODM N=136	Control N=144	P value
Birth length $\geq$ 90th percentile	11.4% (n=22/193)	3.6% (n=7/193)	0.003	11.0% (n=15/136)	5.6% (n=8/144)	0.073
Birth weight $\geq$ 90th percentile	22.8% (n=44/193)	8.3% (n=16/193)	< 0.001	15.4% (n=21/136)	4.9% (n=7/144)	0.003
<b>At age 17 years</b>						
Height (cm)	173.6 $\pm$ 6.3	173.5 $\pm$ 5.9	0.797	161.6 $\pm$ 6.3	161.5 $\pm$ 5.9	0.927
Weight (kg)	69.3 $\pm$ 13.6	66.7 $\pm$ 11.7	0.05	58.9 $\pm$ 13.6	56.2 $\pm$ 9.6	0.06
BMI $\geq$ 85th percentile	26.9% (n=52/193)	16.1% (n=31/193)	0.006	19.1% (n=26/136)	16.0% (n=23/144)	0.296

study goes one step further by analyzing ODM 17 years later. We found that diabetes during pregnancy is a risk factor for male offspring being overweight in adolescence as well. The explanation for this gender difference has not been determined yet. It is possible that, since girls at this age are more concerned about appearance and body weight than boys, they tend to diet more. The role of a plausible epigenetic factor has not been proven.

This is the second report on data for female adolescent offspring of diabetic mothers and supports the earlier study of Tsadok [2]. However, we documented height as well.

Interestingly, our study shows that even though ODM are more prone to be long for gestational age at birth, they are not taller at the end of adolescence.

Our findings suggest that because ODM are prone to being overweight later in life, especially males or those who were born overweight, it is crucial that these children be closely monitored for growth and weight and educated to maintain a healthy lifestyle.

Our study is limited by its retrospective design, such that data on parental weight and height and socioeconomic status were unavailable. In addition, we were able to follow only 75% of the neonates to age 17 years, mostly because of the exemption of several population sectors from military service.

## CONCLUSIONS

Male ODM, mainly those who are born overweight, are at a higher risk of being overweight in late adolescence. There is apparently no effect of being overweight at birth on height in adolescence.

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## Capsule

### Human $\gamma\delta$ T cells are quickly reconstituted after stem cell transplantation and show adaptive clonal expansion in response to viral infection

To investigate how the human  $\gamma\delta$  T cell pool is shaped during ontogeny and how it is regenerated after transplantation of hematopoietic stem cells (HSCs), Ravens and colleagues applied an RNA-based next-generation sequencing approach to monitor the dynamics of the repertoires of  $\gamma\delta$  T cell antigen receptors (TCRs) before and after transplantation in a prospective cohort study. The authors found that repertoires of rearranged genes encoding  $\gamma\delta$  TCRs (*TRG* and *TRD*) in the peripheral blood of healthy adults were stable over time. Although a large fraction of human *TRG* repertoires consisted

of public sequences, the *TRD* repertoires were private. In patients undergoing HSC transplantation,  $\gamma\delta$  T cells were quickly reconstituted; however, they had profoundly altered TCR repertoires. Notably, the clonal proliferation of individual virus-reactive  $\gamma\delta$  TCR sequences in patients with reactivation of cytomegalovirus revealed strong evidence for adaptive anti-viral  $\gamma\delta$  T cell immune responses.

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