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## Original Article

## Body mass index growth trajectories from birth through 24 months in Iranian infants of mothers with gestational diabetes mellitus



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## ABSTRACT

**Aims:** Child growth is one of the important health indicators in pediatric care. Few studies focused on the impact of prenatal exposure to gestational diabetes mellitus (GDM) on growth trajectories particular in early years of childhood. The aim of this study was identifying growth pattern of GDM exposed offspring's, comparison with new WHO child growth standards.

**Methods and materials:** In a population-based Longitudinal study 438 infants exposed to gestational diabetes in utero, aged 0–24 months, born between 2014 and 2016 with at least 9 visits in first 2 years of life were enrolled. Twenty health centers of Ahvaz city (Capital of Khuzestan province, located in south western of Iran) and two referral centers for neonatal hypothyroidism involved the study.

**Results:** Of 438 GDM exposed infants, 54.6% were boys. Incidence of low birth weight and macrosomia were 4.6% and 8.7% respectively.

**Results:** 4.6% had birth weight less than 2500gr and 8.7% was rate of macrosomia. Boys had higher weight and BMI than girls. Peak of BMI was 17.8 ( $\pm 2.07$ ) at 6 months after Gender was significant factor in predicted of BMI growth trajectories in GDM exposed children ( $p = 0.001$ ). BMI in GDM exposed infants, in first 2 years of life was higher than WHO growth standards 2006 ( $P < 0.01$ ).

**Conclusion:** Medians of BMI in GDM exposed infants in all measures was higher than WHO reference data 2006 ( $P < 0.01$ ). Obesity prevention programs must be priority in GDM exposed infants.

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## 1. Introduction

Several evidences emphasized on long-term effects of childhood growth pattern on adult health [1,2]. Faster growth velocity in early life, increases risk of subsequent overweight and obesity [3–5]. Higher BMI during childhood is associated with a higher risk of hypertension, type 2 diabetes mellitus and cardiovascular diseases in adolescence and adulthood [6–8]. Worldwide variation in human growth reported in several countries with different ethnicity [9].

Environmental exposure in utero play essential role in process of growth and development in fetus and later in life [10,11]. Several pregnancy factors have been associated with excess physical

growth in their offspring. Gestational diabetes mellitus (GDM) as any degree of glucose intolerance, onset or first recognition during pregnancy [12], has been suggested as determinant of growth pattern, obesity and related metabolic consequences in exposed offspring's [13,14]. Prenatal exposure to GDM has been linked with higher risk of large size for gestational age and fetal macrosomia [15,16].

Fetal hyperinsulinemia in response to maternal hyperglycemia stimulates fetal growth and regulates food intake and appetite in exposed offspring of mother with gestational diabetes [17–19]. Increasing GDM prevalence due to obesity and type 2 diabetes epidemics raises public health concern related to poor outcomes of the disease in exposed offspring [20,21].

Childhood growth trajectories enable us to monitor growth pattern and to observe start point of overweight and obesity in later years. The World Health Organization (WHO) introduced the new global WHO Child Growth Standards for children under 5 years in

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2006 [22]. The new standards provide a better tool for evaluation of growth and nutrition status in early infancy. Limited studies focused on infancy growth pattern of GDM offspring's and compare it with WHO reference data [23].

Furthermore, short- and long-term outcomes of GDM in offspring are unclear after implementing the IADPSG as a new criterion.

## 2. Methods

In a population-based Longitudinal study, body mass index(-BMI) of 438 infants exposed to gestational diabetes in utero, aged 0–24 months were measured repeatedly. Ahvaz children born between 2014 and 2016 were enrolled in this study. Ahvaz is the capital of Khuzestan province, located in southwestern of Iran with high birth rate [24], high incidence of gestational diabetes [25,26], Persistent Hyperglycemia in women with history of GDM [27,28] and low attendance of this population for postpartum glucose test screening [28,29].

Mothers were undercover of 20 health centers of Ahvaz city or attending 2 referral centers for neonatal hypothyroidism screening between 3 and 5 days after delivery. Infants who had at least 9 visits (Birth, 2,4,6,9,12,15,18 and 24 months) in first 2 years of life included in the analysis. Twin children, newborn with congenital anomaly and offspring of mothers with pre-gestational diabetes were excluded. Birth weight recorded based on vaccination card and next measurements were done by expert bachelors of public health.

Weight of mothers in first and the last month of pregnancy extracted from health records. Gestational age, maternal age, ethnicity and education, job of mother, nutrition status (breast fed, formula or mixed fed), kind of delivery, weight of mothers in first and last months of pregnancy, sex of children and birth rank were studied variable in this survey. International association of diabetes and pregnancy study groups (IADPSG) criteria were used for diagnosis of gestational diabetes; only one abnormal value equal or greater than the introduced threshold value was considered as GDM ( $\geq 92$  mg/dL for fasting glucose or  $\geq 180$  mg/dL for 1-h plasma glucose or  $\geq 153$  mg/dL for 2-h plasma glucose level after drinking 75-gr glucose [30].

Simplified field percentiles tables of WHO (BMI-for-age BOY-S&GIRLS, birth to 2 years) were used for comparison of median values in each visit with a reference data. We used General linear model (SPSS version 22) to analyze repeated measures and to determine related factors of the infants BMI trajectory. Wilcoxon Signed Rank Test was used to compare of medians BMI levels with WHO reference data. Independent 2 samples T-Test was used comparing means of quantitative Variables. We create graphs of medians using Excel software (compare to BMI/aged/sexed medians extracted of WHO simplified tables).

The study was approved by the Research Ethics Committee of the Ahvaz Jundishapur University of medical sciences (D-9205), and written informed consent was obtained from mothers.

## 3. Results

The demographic and clinical characteristics of the GDM exposed infants and their mothers are presented in Table 1. The mean age of mothers was 29.35(SD, 5.19), ranging 17–47 years. Mean weight of mothers in beginning month of pregnancy and last visit were 71.05 kg (SD, 11.95) and 80.52 kg (SD, 12.98) respectively. Of 438 GDM exposed infants, 54.6% were male, 4.6% had birth weight less than 2500gr and 8.7% was rate of macrosomia. Boys had higher weight than girls in all 9 visits from birth through 24 months (Table 2). Average BMIs (SD) at birth, 1 and 2 years were 13.1 (2.46),

17.2 (2.28), and 16.4(2.23) respectively. Peak of BMI was 17.8 ( $\pm 2.07$ ) kg/m<sup>2</sup> and recorded at 6 months after birth (17.9  $\pm$  2.42 kg/m<sup>2</sup> for boys and 17.6  $\pm$  1.72 kg/m<sup>2</sup> for girls). Gender was significant factor in predicted of BMI growth trajectories in GDM exposed children ( $p = 0.001$ ). Fig. 1 shows different pattern of BMI trajectory in boys and girls. Results of Wilcoxon Signed Rank Test showed that median BMI in GDM exposed infants in all measures, in first 2 years of life was higher than WHO reference data 2006 ( $P < 0.01$ ). 3rd, 15th, 50th, 85th and 97th percentile values of BMI by age in GDM exposed (boys and girls) and WHO reference data are presented in Tables 3 and 4. Figs. 2 and 3 show different points of median of BMI/age/sex in studied infants and WHO reference data.

## 4. Discussion

Results of this population-based longitudinal study showed that median BMI in GDM exposed infants in all measures, in first 2 years of life, was higher than WHO reference data 2006 ( $P < 0.01$ ). Also

**Table 1**

The demographic and clinical characteristics of the GDM exposed infants and their mothers.

Gender		
Girl	239	54.6
Boy	199	45.4
Birth Rank		
1	169	38.6
2	162	37
3	76	17.4
$\geq 4$	31	7
Mother education		
Illiterate	19	4.3
Less than high school	120	27.4
High school	210	47.9
Collage	89	89
Mother job		
Housewife	381	87
Occupied	57	13
Mother ethnicity		
Fars	108	24.6
Lor	83	18.9
Arab	247	56.4
Treatment of hyperglycemia in pregnancy		
Diet or nothing	356	81.3
Insulin	58	13.2
Metformin	24	5.5
Kind of delivery		
Vaginal delivery	180	41
Cesarean Section	258	58.9
Preterm delivery	36	8.2
Child nutrition		
Breast feeding	368	84
Formula	21	4.8
mixed	49	11.2

**Table 2**

Mean (SD) of weight (kg) up to 2 years in gestational diabetes exposed infants.

Age of infant(month)	Weight(SD) Boy(N = 199)	Weight(SD) Girl(N = 239)	P value <sup>a</sup>
0	3.358(0.566)	3.258(0.464)	0.04
2	5.359(0.725)	5.174(0.767)	0.01
4	6.874(0.738)	6.652(0.749)	0.002
6	8.116(.855)	7.829(0.728)	<0.001
9	9.029(0.904)	8.737(0.789)	<0.001
12	9.935(1.256)	9.484(1.101)	<0.001
15	10.632(1.146)	10.393(1.279)	0.04
18	11.280(1.555)	11.116(1.343)	0.23
24	12.024(1.726)	11.930(1.571)	0.17

<sup>a</sup> Using independent 2 samples T-Test.

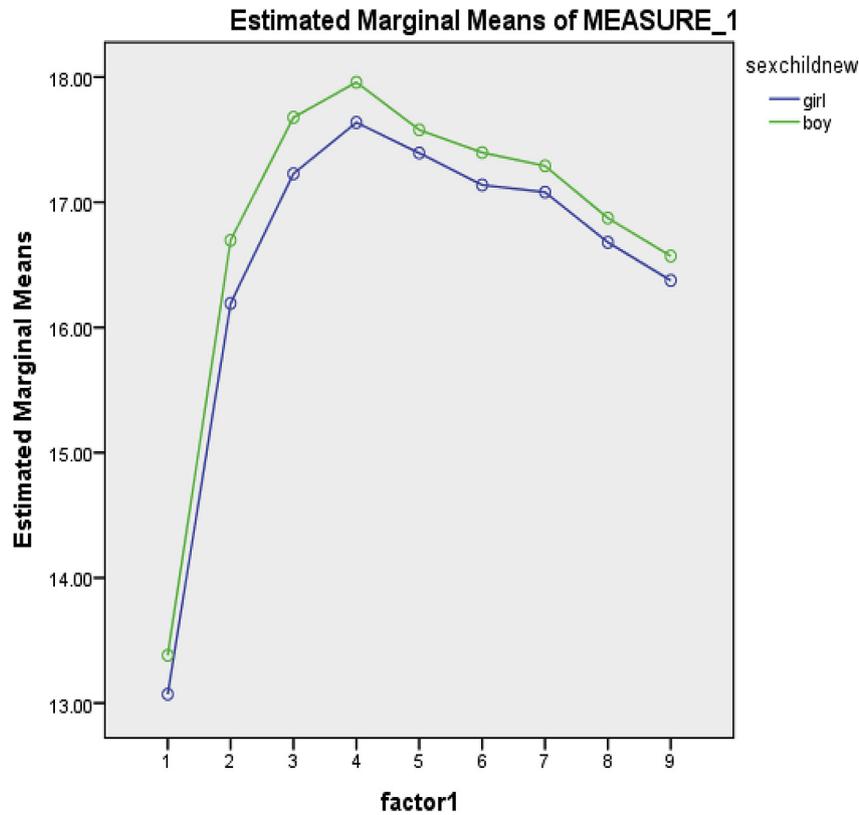


Fig. 1. Mean of BMI in boys and girls at birth, 2,4,6,9,12,15,18 and 24 months of age.

**Table 3**  
3rd, 15th, 50th, 85th and 97th percentile values of BMI by age in GDM exposed boy and WHO reference data.

Age group(months)	3rd GDM exposed	3rd WHO	15th GDM exposed	15th WHO	50th GDM exposed	50th WHO	85th GDM exposed	85th WHO	97th GDM exposed	97th WHO
0	9.61	11.3	11.2	12.2	13.7	13.4	15.3	14.8	17.4	16.1
2	11.0	13.8	15.1	14.9	16.9	16.3	18.1	17.8	20.1	19.2
4	12.8	14.7	15.5	15.7	17.6	17.2	19.4	18.7	23.3	20.1
6	12.9	14.9	14.9	15.9	17.9	17.3	20.3	18.9	22.6	20.2
9	14.2	14.8	16.3	15.8	17.3	17.2	18.9	18.7	21.9	20.1
12	13.3	14.5	15.3	15.5	17.2	16.8	19.4	18.3	23.0	19.6
15	12.6	14.2	15.4	15.2	17.1	16.4	18.6	17.9	21.6	19.2
18	13.0	14.0	14.7	14.9	16.6	16.1	18.5	17.5	22.5	18.8
24	12.4	13.7	14.6	14.5	16.2	15.7	18.7	17.1	21.1	18.3

**Table 4**  
3rd, 15th, 50th, 85th and 97th percentile values of BMI by age in GDM exposed girl and WHO reference data.

Age group(months)	3rd GDM exposed	3rd WHO	15th GDM exposed	15th WHO	50th GDM exposed	50th WHO	85th GDM exposed	85th WHO	97th GDM exposed	97th WHO
0	10.4	11.2	11.4	12.1	12.8	13.3	14.4	14.7	16.6	15.9
2	11.7	13.2	14.2	14.3	16.5	15.8	18.1	17.4	19.6	18.8
4	12.8	14.0	14.9	15.2	17.4	16.7	18.9	18.3	22.0	19.8
6	14.2	14.3	16.0	15.4	17.5	16.9	19.2	18.6	20.7	20.1
9	11.7	14.2	15.4	15.3	17.4	16.7	19.5	18.4	21.0	19.9
12	13.2	13.9	14.7	15.0	16.9	16.4	19.4	17.9	22.0	19.4
15	14.3	13.7	15.1	14.6	16.9	16.0	18.9	17.5	21.7	19.0
18	12.8	13.4	14.8	14.4	16.6	15.7	18.3	17.2	21.6	18.6
24	12.4	13.2	14.4	14.1	16.0	15.4	18.4	16.9	20.5	18.2

gender was significant factor in predicted of BMI growth trajectories in GDM exposed children.

Accelerated BMI growth following prenatal gestational diabetes exposure reported in some studies. Inconsistent with our results, most of them suggest that effect of GDM on BMI growth starting in

late childhood. In other hand, GDM may have a delayed role on growth pattern of offspring's [31,32]. Dabelea and colleagues found that there is no differences in mean BMI among Pima Indian exposed to diabetes in utero healthy children at ages 5–8 years, but they reported higher BMI levels in exposed offspring's at 9–12

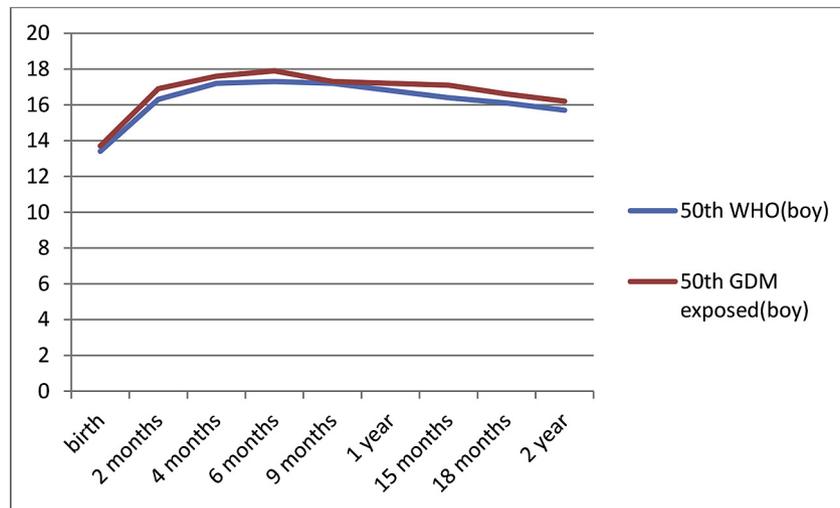


Fig. 2. Median values of BMI by age in GDM exposed boy and WHO reference data.

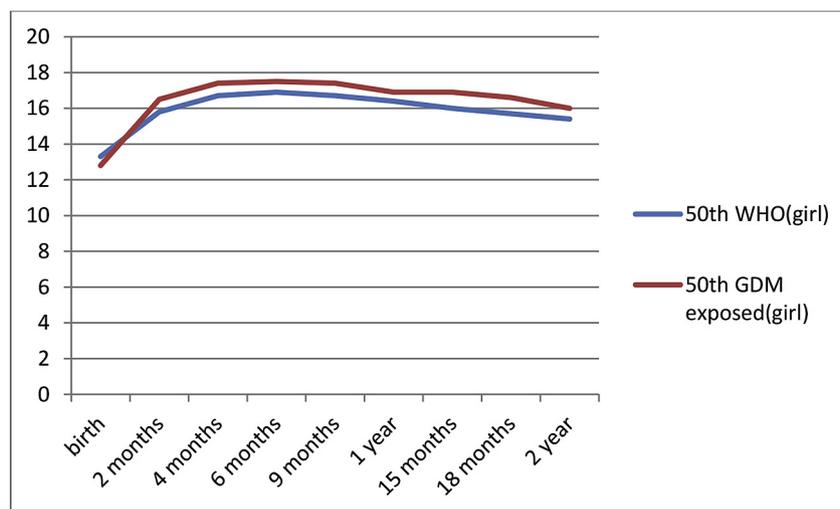


Fig. 3. Median values of BMI by age in GDM exposed girl and WHO reference data.

years of age [33].

Crume et al. [34] In a multi-ethnic population from Colorado, found that the overall BMI growth trajectory was not significant from birth through 26 months of age ( $p = 0.48$ ). But from 27 months of age through 13 years ( $p = 0.008$ ) significantly different for exposed and unexposed subjects were detected. However, Results of a randomized clinical trial, done by Gillman et al., in Australia showed that offspring's of mothers with mild after treatment of hyperglycemia in pregnancy have not different growth pattern at 4–5 years of age [35]. Baptiste-Roberts and colleague reported no relationship between GDM exposed and offspring weight at ages 3 and 4. But children of mothers with GDM were 0.46 kg heavier at age 7 than children of mothers without gestational diabetes [31].

Almost all of mentioned studies had national control group. We compared our data with WHO growth standards. Although more than 100 countries adopted new WHO data and curves [36], Many recent studies in various socio-economic population, reported different pattern of growth from WHO means [9].

For final judgment we must compare data from ahvazin healthy infants with data from the WHO growth standards. It may be

possible that the results of this study represent different pattern of growth in studied population with WHO reference data. Role of GDM as predictor of obesity in early childhood needs more researches.

Gender identified as a predictor of growth pattern in this study. Significant effect of gender on physical growth reported in previous studies. Boys have higher weight, height and head circumference at birth and the first year of life. Hormonal differences such as growth hormone, may because of differences of growth pattern between boys and girls [37,38].

Lack of data from healthy infants was the most important limitation of this study. Our data sheet of unexposed infants was not ready for analysis. We will use them in next report of this study. The first longitudinal population-based on growth pattern of Iranian GDM-exposed offsprings and considerable sample size are strengths of this study.

#### Conflict of interest

No conflict of interest.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.dsx.2018.10.002>.

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