Impaired Postnatal Growth of Infants Prenatally Exposed to Cigarette Smoking

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Most of the previous studies have shown a significant inverse relationship between smoking during pregnancy and weight, height and head circumference of infants at birth, but there is limited literature that assesses the head circumference measures of infants of smoker mothers in postnatal follow-up. The aim of this study was to assess the effects of maternal smoking and passive smoking during pregnancy on postnatal anthropometric measures of infants. Infants were divided into 3 groups: infants of smokers (n = 48), passive smokers (n = 57) and nonsmokers (n = 54), and were evaluated for their weight, height and head circumference at birth, 3 months and 6 months of age. Infants of smokers showed significant weight and head circumference deficits at birth compared to nonsmokers’ infants (p < 0.05 and p < 0.001, respectively). At 6 months of age, infants of smokers continued to show significant deficits in all 3 measures compared to nonsmokers’ infants (p < 0.001 for each), and infants of passive smokers showed only marginal decreases. Moreover, the weight and height growth velocities of the smokers’ infants remained deficient, whereas their growth velocity of the head circumferences increased from birth up to 6 months and reached the growth velocity of the nonsmokers’ infants. Infants of passive smokers showed a complete catch-up growth at 6 months. This study indicates that smoking during pregnancy results in serious deficits in infants’ growth even after birth. Therefore, it is essential to inform smoker women before pregnancy the possible growth retardation of infants. ——— maternal smoking; infant growth; passive smoking; antenatal tobacco exposure; birth outcome.

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Maternal smoking during pregnancy is known to affect both physical and intellectual growth of infants (Conter et al. 1995; Cornelius et al. 1995; Cornelius et al. 2002; Steyn et al. 2006; Vielwerth et al. 2007; Hindmarsh et al. 2008). It has also been considered as an important risk factor for intrauterine growth retardation (Ingvarsson et al. 2007; Aagaard-Tillery et al. 2008). Most of the previous studies reveal that mothers who smoke during their pregnancies deliver infants weighing from 100 g to 300 g less than babies born to nonsmoking mothers (Conter et al. 1995; Cornelius et al. 1995, Cornelius et al. 2002). On the other hand, some of these studies show a significant inverse relationship between tobacco use and height and head circumference at birth (Hardy and Mellits 1972; Cornelius et al. 1995; Ong et al. 2002; Vielwerth et al. 2007; Hindmarsh et al. 2008). These growth measures at birth, decrease in direct proportion to the number of cigarettes smoked per day (Conter et al. 1995; Cornelius et al. 1995; Vielwerth et al. 2007; Aagaard-Tillery et al. 2008).

There have been many studies investigating the effect of gestational cigarette smoking on weight, height and head circumference at birth (Conter et al. 1995; Ong et al. 2002; Ingvarsson et al. 2007; Vielwerth et al. 2007; Ward et al. 2007), but only a few studies analyzed the weight and height follow-up of children born to mothers who smoked during their pregnancies (Vaglenova et al. 2004; Steyn et al. 2006). There have been even fewer studies in the literature for head circumference follow-up of these children which is an important indicator of the brain development (Hindmarsh et al. 2008). Also, there are controversial ideas in the literature about the effect of passive smoking during pregnancy on growth measures of newborns. Some of the studies claimed a significant reduction in growth measures of infants by passive smoking (Ward et al. 2007), whereas others found that passive smoking did not affect birthweight significantly (Steyn et al. 2006; Wu et al. 2007). Our study is unique in that we aimed to demonstrate the effect of both maternal smoking and passive smoking during pregnancy on anthropometric measures of the babies mainly their head circumferences at birth and postnatally in infancy.

Nicotine affects brain development through its actions on nicotinic acetylcholine receptors (nAChRs) and it mim-
ics the neurotransmitter acetylcholine via its actions on nAChRs which act to initiate, prolong or enhance the release of a number of neurotransmitters including dopamine, acetylcholine, norepinephrine, serotonin, glutamate and GABA (Eppolito and Smith 2006; Pauly and Slotkin 2008). As neurotransmitters act as critical differentiation signals during nervous system development, coordinating the cellular and architectural assembly of the brain, nicotine is claimed to inversely affect nervous system development (Pauly and Slotkin 2008). Consequently, deficits in neuropsychological development on tasks that require learning, memory, and problem solving skills are impaired in children up to age 10 following exposure to maternal smoking during gestation (Cornelius et al. 2002).

Infant growth which is largely a continuation of in utero growth, is influenced predominantly by factors determining intrauterine growth and nutrition, and is growth hormone independent, whereas growth during childhood is largely growth hormone dependent (Hindmarsh et al. 2008). Therefore, catch-up growth in the first 6 months of life is related to poor intrauterine growth and is also influenced by postnatal food availability but it is unlikely to be mediated through the growth hormone axis. Finally, assessing the growth process over a period of time longer than 6 months introduces a confounding variable, which is the timing of the switch to growth hormone dependent growth and which clinically begins at varying time points after 6 months of age (Hindmarsh et al. 2008). Hereby, it is logical to follow infants up to 6 months of age in order to see solely the effect of cigarette smoking independent of the effect of growth hormone.

This study aimed to investigate the postnatal effects of maternal smoking and passive smoking during pregnancy on growth measures of infants during the first 6 months of life in a longitudinal cohort of individuals studied from the first trimester of pregnancy. We wanted to underline the necessity for public policies created to help pregnant women for quitting smoking.

Methods

Two hundred eighty-eight pregnant women who applied for antenatal examinations within a month at Sisli Etfal Education and Research Hospital, Istanbul, Turkey were recruited for this study. The participants filled out a detailed written questionnaire while attending antenatal services and their consent was taken along with the questionnaire. Data on their smoking habits, education periods by years (no education, 1-5 years of primary school education, secondary school or higher education), economic status determined by the monthly income (low class: min. wage or lower, high class: 2000.-TL or more, middle class: from min. wage up to 2000.-TL), parity, age, prepregnancy weight and height, paternal height and household members’ smoking habits were obtained from this questionnaire. Mothers’ weight gain was noted at each antenatal visit. The delivery room interview ascertained the information about mothers’ smoking habits. Mothers were asked how many cigarettes they smoked per day. If they had quit smoking, they were asked when and how many cigarettes they smoked per day before they quit. The household members’ smoking habits were also ascertained in the delivery room interview. Passive smokers were defined only from those who had a household member who smoked more than 10 cigarettes per day inside the house.

Out of 288, 19 newborns who were babies of diabetic mothers, multiple pregnancies, complicated pregnancies; babies born with a congenital abnormality and preterm babies were excluded from the study. The 269 newborns who were found to be eligible for the study, were called for 3rd and 6th month control exams. Only 159 of 269 newborns, attended both 3rd and 6th month control exams and were considered for the study. Of these 159 babies, 48 were babies of smokers, 57 were babies of passive smokers and 54 were babies of nonsmokers. Among the 48 smoker mothers, 37 of them smoked less than 10 cigarettes per day and 11 of them smoked more than 10 cigarettes per day.

Measurements and Follow-Up

The initial examination of newborns conducted within the first 24 hours after birth included birthweight, height, head circumference and Apgar scoring. Gestational age was calculated by Naeyege formula. Infants were weighed naked on a beam balance to the nearest 10 g using standard techniques. Crown-to-heel lengths were measured on a portable measuring board to the nearest 0.1 cm and their head circumference was measured with a disposable tape to the nearest 0.1 cm at the longest occipitofrontal circumferences.

At their control visits, infants’ weights, heights and head circumferences were taken, their complete physical examination and assessment of nutritional status were done, and mothers were given necessary advices about baby care and feeding. These examinations of infants were done always by the same investigator (A.K.F.). Our babies were totally breast-fed until 3 months of age and at 4-month examination, mothers were given information of how to start solids and food supplements. Those who were weaning of breast milk or who needed more supplements were introduced formula.

The ethical approval for this study was taken from the ethics committee of Sisli Etfal Education and Research Hospital.

Statistical Analysis

For statistical analysis, the Kruskal–Wallis test was used for the parametric variables in Table 1. Nonparametric categorical data such as mother’s education level and the economic status of the family were compared using the Chi-square test (Table 2). To compare the weights, heights and head circumferences at birth, 3 and 6 month of age, differences in group means were analyzed by the ANOVA (Tables 3 and 4) and the Dunnett t test (Table 2). Data were reported as mean ± standard deviation (SD) with 95 % confidence intervals when appropriate in Table 2. F values are given for the ANOVA test in Tables 3 and 4. P values less than 0.05 were considered statistically significant. The statistical analyses were performed using the SPSS software, version 16.0 for Windows.

Results

Table 1 and 2 show the descriptive statistics for infants and their parents. There was no statistical difference between the smokers’ (n = 48), passive smokers’ (n = 57) and nonsmokers’ (n = 54) groups in terms of maternal and paternal age, maternal and paternal height, maternal parity, prepregnancy weight and weight gain during pregnancy. Only mothers’ education showed differences between
groups ($p < 0.001$) (Table 2). The smokers seemed to be the group with either higher education status or no education status compared to nonsmokers. The infant groups were similar with respect to gender and gestational age. Apgar scoring for all groups were within normal values (5' Apgar: 9.76, 9.49 and 9.71 respectively).

Table 3 shows the anthropometric measures at birth, 3 and 6 months control visits of infants born to nonsmokers, smokers and passive smokers. No significant difference was detected between mean and median variables, and therefore only mean weights, heights and head circumferences were presented. The mean birthweight was 3,445.37 g in infants of nonsmokers and 3,198.96 g in infants of smokers. The difference ($−246.41$ g) was statistically significant ($p < 0.05$). Also, infants of passive smokers were found to have a birthweight difference of $−66.42$ g with infants of nonsmokers, but this difference was not statistically significant.

Birth height differences between groups were not statistically significant. But, when we compared newborns’ head circumferences at birth, the difference between infants of smoker and nonsmoker mothers was $−1.26$ cm, which was a significant deficit ($p < 0.001$). In contrast, the difference of head circumference at birth between the infants of passive smokers and nonsmokers ($−0.42$ cm) was not statistically significant (Table 3).

Infants of smoking mothers kept showing significant deficits of weight at 3 and 6 months. The weight difference between infants of smokers and nonsmokers at the 3-month visit was $−684.27$ g and at the 6-month visit, the deficit increased to $−753.12$ g. Both of the deficits were statistically significant ($p < 0.001$). Infants of passive smokers also showed weight deficits at 6th month control examination compared to babies of nonsmokers ($−130.43$ g), but it was not statistically significant (Table 3).

Height deficit of infants of smokers, which was $−2.99$ cm.
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At the 3-month control visit, decreased to −1.98 cm at 6 months. Both of the deficits were statistically significant (p < 0.001). The difference of head circumference between infants of smoking mothers and infants of nonsmokers also showed the significant reduction at 3 and 6 months (−1.66 cm and −0.88 cm respectively) (p < 0.001) (Table 3).

At the 6-month control examination, the height and head circumference deficits of infants of passive smokers were found to have height and head circumference deficits reduced to −0.59 cm and −0.33 cm, respectively (Table 3). These results were not statistically significant.

Table 4 shows the growth velocities from birth up to 6 months of age in infants of the 3 groups. The growth velocity is the mean difference of weight, height and head circumference measures at 3 and 6 months of age and the measures at birth. The differences of growth speed in weight and height from birth up to 6 months of age between infants of smoker mothers and nonsmokers were highly significant (p = 0.000 and p = 0.004); namely, infants born to smoker mothers and passive smokers had a lower growth velocity of weight and height in the first six months of life. Although the weight and height growth velocities of the smokers’ infants remained deficient compared to nonsmokers’ infants, the head circumference growth velocity of the nonsmokers’ infants (p > 0.05) (Table 4).

Table 5 shows the growth velocity from birth up to 6 months of age in infants by the number of cigarettes smoked per day. When the weight and height growth velocities in infants of mothers who smoked more than 10 cigarettes per day were compared with the growth velocity of the infants of nonsmokers and passive smokers, the deficits were found to be significant. But, the head circumference growth velocity in infants born to mothers who smoked more than 10 cigarettes per day reached the head circumference growth velocity of infants of nonsmokers and passive smokers at 6 months of age postpartum (p = 0.482) (Table 5).

**Discussion**

The present study indicated that smoking during pregnancy results in significant deficits in birthweight and height, and these deficits continue to be seen in infants of smokers at 6 months of age since their growth velocity in weight and height remain deficient. Also, this study demonstrated that head circumference of the infants of smokers shows deficits from birth until 6 months of age compared to infants of smokers but the head growth velocity of the head circumference of these infants increased constantly from birth up to 6 months of age. Our study is unique with respect to the findings in postnatal head circumference follow-up of infants of smokers. We also revealed that
### Table 3: Comparison of the infants’ weights, heights and head circumferences between the groups at birth, 3 and 6 months of age.

<table>
<thead>
<tr>
<th></th>
<th>Birth Mean (g)</th>
<th>Birth differences (g)</th>
<th>3rd month Mean (g)</th>
<th>3rd month differences (g)</th>
<th>6th month Mean (g)</th>
<th>6th month differences (g)</th>
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<tbody>
<tr>
<td><strong>Weight (g)</strong></td>
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<tr>
<td>Nonsmokers (n = 54)</td>
<td>3445.37 (461.36)</td>
<td>−66.42 [−271.33, 138.48]</td>
<td>6661.67 (806.46)</td>
<td>−378.16 [−708.21, −48.10]</td>
<td>8339.17 (922.46)</td>
<td>−130.43 [−501.36, 240.50]</td>
</tr>
<tr>
<td>Passively smokers (n = 57)</td>
<td>3378.95 (520.55)</td>
<td></td>
<td>6283.51 (729.52)</td>
<td></td>
<td>8208.74 (861.60)</td>
<td></td>
</tr>
<tr>
<td>Smokers (n = 48)</td>
<td>3302.41 (520.55)</td>
<td></td>
<td>5977.40 (777.00)</td>
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<td>7586.04 (835.50)</td>
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<tr>
<td><strong>Height (cm)</strong></td>
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<tr>
<td>Nonsmokers (n = 54)</td>
<td>49.62 (2.38)</td>
<td>−0.32 [−1.22, 0.57]</td>
<td>64.53 (3.38)</td>
<td>−2.26 [−3.61, −0.91]</td>
<td>69.50 (3.02)</td>
<td>−1.98 [−3.18 to −0.78]</td>
</tr>
<tr>
<td>Passively smokers (n = 57)</td>
<td>49.30 (1.96)</td>
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<td>62.26 (2.98)</td>
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<td>68.91 (2.37)</td>
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<tr>
<td>Smokers (n = 49)</td>
<td>49.10 (1.97)</td>
<td></td>
<td>61.54 (3.10)</td>
<td></td>
<td>67.52 (2.72)</td>
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<tr>
<td><strong>Head circumference (cm)</strong></td>
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</tr>
<tr>
<td>Nonsmokers (n = 54)</td>
<td>35.02 (1.49)</td>
<td>−0.42 [−1.09 to 0.44]</td>
<td>43.69 (1.19)</td>
<td>−0.33 [−0.84, 0.17]</td>
<td>43.36 (0.99)</td>
<td>−0.88 [−1.41 to −0.35]</td>
</tr>
<tr>
<td>Passively smokers (n = 57)</td>
<td>34.60 (1.35)</td>
<td></td>
<td>40.42 (1.25)</td>
<td></td>
<td>43.36 (1.30)</td>
<td></td>
</tr>
<tr>
<td>Smokers (n = 48)</td>
<td>33.70 (1.13)</td>
<td></td>
<td>41.58 (1.62)</td>
<td></td>
<td>42.51 (1.22)</td>
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</table>

Significance of difference (in bold). (CI, Confidence Intervals)

- $p < 0.01$ for passive smokers vs. nonsmokers
- $p < 0.001$ for smokers vs. nonsmokers
- $p < 0.0001$ for smokers vs. nonsmokers

**Gestational Smoking and Postnatal Growth**

Maternal smoking during pregnancy has long been considered an important risk factor for growth retardation (Ingvarsson et al. 2007; Aagaard-Tillery et al. 2008). This association was first reported in 1957 and has been proven in numerous subsequent studies (Conter et al. 1995; Cornelius et al. 1995, Cornelius et al. 2002; Steyn et al. 2006; Vielwerth et al. 2007; Hindmarsh et al. 2008). Previous studies have found a remarkably constant 100-300 g difference in birthweight between cigarette smokers’ and nonsmokers’ infants (Conter et al. 1995; Cornelius et al. 1995, Cornelius et al. 2002). The difference in our study (−246.41 g) was within the same range. Usually, the birth height and head circumference of infants born to mothers who smoked during their pregnancies were found to be respectively, 1-1.5 cm and 0.2-1 cm less than the measures of infants born to nonsmokers (Hardy and Mellits 1972; Cornelius et al. 1995; Ong et al. 2002; Ingvarsson et al. 2007; Ward et al. 2007; Hindmarsh et al. 2008). In our study, birth height differences between groups were not statistically significant and the birth height difference between smokers’ and nonsmokers’ infants (−0.52 cm) was below the range suggested in these articles. But, we showed that there was an important difference in head circumference of infants born to mothers who smoked during their pregnancies (−1.26 cm) compared to nonsmokers’ infants.

Previously published studies of passive smoking during pregnancy indicate a small decrease in birthweight among the newborns. The size of the effect found is a 28 g reduction in birthweight according to most of these studies (Steyn et al. 2006). However, Ward et al. (2007) found a significant decrease (−36 g) in birthweight between the women not exposed and those exposed to environmental tobacco smoke. In our study, compared to infants who were not exposed, infants who were exposed to environmental tobacco smoke antenatally, were found to have deficits in weight (−66.42 g), height (−0.32 cm) and head circumference at birth (−0.42 cm), none of which were statistically significant. Our babies kept showing minimal deficits in these growth parameters until 6 month of age postpartum, but they showed a significantly high growth velocity from birth to 6 month postpartum in both weight and height compared to nonexposed babies (Table 4).

All these effects of antenatal smoking are also influenced by maternal age and parity, parental educational and socioeconomic level, maternal and paternal height, prepregnancy weight and weight gain during pregnancy, and by some obstetric complications (Conter et al. 1995; Cornelius et al. 2002; Steyn et al. 2006; Hindmarsh et al. 2008; Aagaard-Tillery et al. 2008). Thus, records of risk factors for intrauterine growth restriction and knowledge of possible associations between specific risk factors, pre- and postnatal growth patterns and specific parental health
parameters would assist in the interpretation of our findings. For this purpose, newborns who were babies of diabetic mothers, multiple pregnancies, complicated pregnancies; babies born with a congenital abnormality and preterm babies were excluded from our study. The profile of the women who used tobacco products during pregnancy identified two target groups for intervention. The cigarette smokers seemed to be the group with either higher education status or no education status compared to nonsmokers in our study. There weren’t any statistically significant differences in other demographic parameters.

The postnatal effects of prenatal tobacco exposure on the growth of exposed offsprings are not as clear. Recent studies done for this purpose proved that the negative association between growth measures at birth and prenatal cigarette exposure was overcome within the first 12 months of life and most of these studies revealed that postnatal growth of weight and height was accelerated in the infants of heavy smoking mothers during the first 6 months of life where as head circumference of these infants remained retarded for longer period of time. Among infants who showed catch-up growth, males caught up more rapidly than females in these studies (Conter et al. 1995; Ong et al. 2002; Vaglenova et al. 2004; Vielwerth et al. 2007; Hindmarsh et al. 2008).

Vielwerth et al. (2007) observed that maternal smoking during pregnancy restricts prenatal growth of both weight and height, whereas their postnatal growths are accelerated. In our study, both 3rd month and 6th month weights and heights of infants born to smokers showed significant deficits compared to infants of nonsmokers and their growth velocities within the first 6 months of life were lower than infants of nonsmokers. Ong et al. (2002) found out that babies who were born to smokers and who were breast-fed show slower weight and height gain than bottle-fed babies born to nonsmokers and they observed that the growth-limiting effects of breast-feeding continues well beyond infancy. Breast-feeding may be a contributing factor in our study for the persistence of the deficits in the birthweight and height at 6th month of age because breast milk protects the individual from excessive or rapid weight gain during the first 6 months of life (Hindmarsh et al. 2008). But recent data suggest protective effects of breast-feeding against later childhood obesity which is known to occur as a longer-term effect of maternal smoking (Cornelius et al. 2002; Ong et al. 2002; Eppolito and Smith 2006).

We also observed that the deficit in birth head circumference of smokers’ infants persisted at 6 month postpartum but head circumference growth velocity remained same in both smokers and nonsmokers group. This finding underlined the importance of head circumference measurement in infants of smoking mothers since cigarette use during pregnancy has been correlated with decreased Intelligence Quotient scores, behavioral disorders and neurological deficits (Vaglenova et al. 2004; Eppolito and Smith 2006).

As a conclusion, data from this study indicated that

### Table 4. Comparison of growth velocities from birth up to 6 months of age by mothers’ smoking habits.

<table>
<thead>
<tr>
<th></th>
<th>Nonsmoker (n = 54)</th>
<th>Passive smokers (n = 57)</th>
<th>Smokers (n = 48)</th>
<th>F</th>
<th>P</th>
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<tbody>
<tr>
<td><strong>Weight (g) difference</strong></td>
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</tr>
<tr>
<td>From birth to 3(^{rd}) month</td>
<td>3242.37 (850.99)</td>
<td>2927.91 (714.85)</td>
<td>2701.46 (688.93)</td>
<td>6.443</td>
<td>&lt; 0.01¹</td>
</tr>
<tr>
<td>From birth to 6(^{th}) month</td>
<td>5010.07 (888.55)</td>
<td>4781.74 (818.08)</td>
<td>4287.11 (762.91)</td>
<td>9.061</td>
<td>&lt; 0.001²</td>
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<tr>
<td><strong>Height (cm) difference</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>From birth to 3(^{rd}) month</td>
<td>14.63 (3.52)</td>
<td>12.75 (3.25)</td>
<td>12.05 (2.63)</td>
<td>8.884</td>
<td>&lt; 0.001¹</td>
</tr>
<tr>
<td>From birth to 6(^{th}) month</td>
<td>20.02 (3.04)</td>
<td>19.53 (2.52)</td>
<td>18.10 (2.92)</td>
<td>5.644</td>
<td>&lt; 0.01²</td>
</tr>
<tr>
<td><strong>Head circumference (cm) difference</strong></td>
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</tr>
<tr>
<td>From birth to 3(^{rd}) month</td>
<td>6.24 (1.72)</td>
<td>5.76 (1.40)</td>
<td>6.00 (1.37)</td>
<td>1.315</td>
<td>NS²³</td>
</tr>
<tr>
<td>From birth to 6(^{th}) month</td>
<td>8.53 (1.32)</td>
<td>8.75 (1.39)</td>
<td>8.82 (1.34)</td>
<td>0.564</td>
<td>NS²³</td>
</tr>
</tbody>
</table>

*NS, Not significant.
¹Nonsmokers vs. Passive smokers.
²Nonsmokers vs. Smokers.
³Passive smokers vs. Smokers.
maternal smoking and passive smoking during pregnancy were associated with weight and height deficits at birth which were not overcome by 6 months after birth. Head circumference followed a similar trend, although the effect was less marked than with weight and height because there was a compensatory postnatal growth in head circumference in contrast to weight and height. Data from this study indicate that smoking during pregnancy results in serious deficits in infants’ growth even after birth especially on head circumference which is an indicator of the brain development. Therefore, it is essential to reach out the women before pregnancy and use these data to inform public policy.

References


Ingvarsson, R.F., Bjarnason, A.O., Dagbjartsson, A., Hardardottir,


