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Maternal hormone levels and perinatal characteristics: implications for testicular cancer

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Abstract

Purpose—It has been hypothesized that the risk of testicular germ cell tumors (TGCT) is associated with maternal hormone levels. To examine the hypothesis, some studies have used perinatal factors as surrogates for hormone levels. To determine the validity of this assumption, hormone-perinatal factor relationships were examined in the Collaborative Perinatal Project.

Methods—Maternal estradiol, estriol and testosterone levels in first and third trimester serum samples were correlated with perinatal factors among 300 mothers representative of populations at high (white Americans) or low (black Americans) risk of TGCT.

Results—Among white participants, testosterone levels, were negatively associated with maternal height ($p<0.01$) and age ($p=0.02$), and positively associated with maternal weight ($p=0.02$) and BMI ($p<0.01$), while estradiol levels were negatively associated with height ($p=0.03$) and positively associated with son's birthweight ($p=0.04$). Among black participants, estriol levels were negatively associated with maternal weight ($p=0.01$), BMI ($p=0.02$) and gestational age ($p<0.01$), and positively associated with son's birthweight ($p<0.01$), length ($p=0.04$) and head circumference ($p=0.03$).

Conclusions—These findings indicate that the use of perinatal characteristics as surrogates for hormone levels should be limited to a specific ethnic group. Among white men, previously reported associations of TGCT with maternal weight and age may be due to lower maternal testosterone levels.

Keywords

testicular cancer; maternal hormones; perinatal factors

Introduction

There is increasing evidence that testicular germ cell tumors (TGCT) originate *in utero* (1). Although the mechanism that increases risk is unknown, it has been suggested that an imbalanced intrauterine hormonal milieu may be important (2-4). It is very difficult, however, to study the association between a fetal exposure that is not routinely measured, such as hormone levels, and a disease that occurs decades later. To overcome this problem, some studies have examined the relationship between perinatal variables and TGCT, under the assumption that the perinatal variables are good surrogate measures of *in utero* hormonal conditions.

To test the validity of this assumption, several studies have examined the relationships between perinatal factors and maternal hormone levels (5-11). Some of these studies, however, have included hormone samples from only one time in pregnancy or studied members of only one ethnic group. In addition, almost all studies to date have included mothers pregnant with both male and female fetuses. As relationships between perinatal factors and maternal hormones may vary by sex of the fetus or by ethnic group, further scrutiny of these relationships was indicated.

With the goal of informing future studies of TGCT, the relationships between perinatal factors and maternal hormone levels were examined in mothers pregnant with male fetuses. The mothers were selected to represent populations at differing risks of TGCT: white Americans (high risk) and black Americans (low risk) to determine whether perinatal factor-hormone relationships vary by ethnicity. In addition, the relationships were examined in samples drawn in first and third trimesters, as these are the critical time periods for testicular descent, the failure of which is strongly associated with risk of TGCT (12).

Methods

Study Population

A detailed description of the study population has been previously reported (13). Briefly, 150 pairs of black and white mothers were selected from among the participants of the Collaborative Perinatal Project (CPP). The CPP cohort study was designed to examine perinatal risk factors for neurologic disorders among offspring (14). Pregnant women were enrolled at 12 medical centers in 11 U.S. cities (Baltimore, Boston, Buffalo, Memphis, Minneapolis, New Orleans, New York (two centers), Philadelphia, Portland, Providence and Richmond) between 1959 and 1965. At 11 study centers, patients were recruited from the participating university hospital's prenatal care clinic, and in one study center (Buffalo), patients were recruited from 13 participating private medical practices. The method of participant selection varied across study centers. For example, at Columbia-Presbyterian Medical Center, every sixth woman who was potentially eligible was invited to participate; at Charity Hospital in New Orleans, potentially eligible women were selected if their patient identification number ended in zero; and in Boston, all potentially eligible women were invited to participate. Women were ineligible if they were incarcerated, if they were planning to leave the area or give up the child for adoption, or if they gave birth on the day they were recruited into the study. Records of the number of women who refused to participate at baseline were not kept, but participation rates were assumed to be high (e.g., the rate was >99% at the Johns Hopkins center in Baltimore (Janet Hardy, Johns Hopkins University, personal communication, 2001)). The characteristics of women in the sample at registration were essentially the same as those in the sampling frame (14). Four percent of subjects who enrolled were lost to follow-up before delivery.

The mothers donated non-fasting blood samples at approximately eight-week intervals throughout their pregnancies, as well as at delivery and 6 weeks postpartum. All serum samples have been subsequently stored in glass vials at -20°C , with no recorded thaws. Details of all clinic visits were recorded in the study records. The maternal characteristics of interest to the current analysis (age, height, pre-pregnancy weight, smoking and socio-economic index) were obtained from the women at the time of enrollment in the study. The neonatal characteristics (length of gestation, birth weight, birth length, head circumference) were obtained in the delivery room. Approximately 42,000 women were enrolled in the study, and 55,000 children were born into the study. The children were systematically assessed, at regular intervals, for the presence of birth defects and other outcomes through the age of 7 years. Follow-up to age 7 years was completed for approximately 75 percent of subjects born into the study.

Mothers were selected for the current study based on the following criteria: pregnant for the first time, gave birth to a singleton male infant who lived at least one year, length of gestation between 26 and 48 weeks, had blood samples available from both first and third trimesters, babies' birthweight was at least 500 grams, and baby had no diagnoses of undescended testes, late descending testes, retractile testes or other malformations possibly related to maternal hormone levels (i.e., CNS and related musculoskeletal, genitourinary, inguinal hernia, hydrocele, supernumerous nipples). The study was limited to mothers pregnant for the first time because estrogen levels have been reported to be higher in first pregnancies (10, 15), and because some studies have linked TGCT risk to birth order (16, 17).

A total of 162 black and 652 white mothers satisfied the study inclusion criteria. The principal limiting criterion was the availability of first trimester samples as the median entry time into the study for the whole CPP population was 20 weeks gestation. In addition, the nulliparity criterion restricted the study group to approximately one third of the whole population. Each of the 162 black mothers was matched to a white mother on the closest blood draw gestational age dates. The matches were then reordered to select the 150 pairs best matched on draw dates. Among the 300 mothers selected, the gestational ages ranged between 30 and 43 weeks.

Laboratory Assays

Serum hormone levels were assessed at the Reproductive Endocrine Research Laboratory of the University of Southern California Keck School of Medicine (13). Unconjugated estriol, unconjugated estradiol and testosterone were determined by well-established, validated radioimmunoassay methods that are carried out routinely in the laboratory (18, 19).

Study samples, labeled with unique, random identification numbers, were analyzed in 17 batches. Each batch contained four quality control samples that had been aliquoted from a single blood pool. The intra-assay coefficients of variation ranged between 3.7% and 12.6%, while the inter-assay coefficients of variation ranged between 4.8% and 13.3%.

Statistical Analysis

Distributions of perinatal characteristics were compared using chi-square tests. Small-for-gestational age (SGA) was determined by comparing birthweight for each gestational age in weeks in the CPP to the 10th percentile of birthweight for gestational age developed by William's et al. for California white Non-Hispanic (20) and black births (R.L. Williams, personal communication) which occurred between 1970-1976. Tertile categories of birth length, head circumference, and maternal pre-pregnancy weight were based on the distribution in the entire study population. Hormone ratios were calculated by dividing total

estradiol and estriol by total testosterone. Multiple linear regression modeling was used to estimate the mean change in hormone levels or hormone ratios for an increase of one standard deviation in maternal characteristics including age, height, pre-pregnancy weight, body mass index, and number of cigarettes smoked during pregnancy, adjusting for gestational age at blood draw and socioeconomic index. The adjustment for gestational age at blood draw was employed because the variable was used as a matching factor in the study design. Results did not differ between models using original hormone levels and models using log-transformed levels. The results of models using original levels are presented below. The standard deviation for each maternal characteristic was calculated from the entire population. Multiple linear regression modeling was also employed to estimate the mean change in birthweight, birth length, head circumference, and gestational age for an increase of one standard deviation in maternal hormone levels or one unit change of the hormone ratios, adjusting for gestational age at blood draw, age, pre-pregnancy weight, height, cigarette smoking during pregnancy, and socioeconomic index. Because of pronounced correlations between birthweight and birth length ($r=0.71$), birthweight and head circumference ($r=0.64$), and birth length and head circumference ($r=0.51$), each variable was not adjusted for the other when the linear regression models of the relationship between birth size and hormone levels were fit. Interactions were assessed by including product terms between pairs of variables in the regression models and were then examined using t-tests. All tests of significance were two-sided. Analyses were performed using SAS software, version 8.02 (SAS Institute, Inc., Cary, NC).

Results

Black mothers were significantly more likely than white mothers to be younger ($p<0.0001$), of lower social economic status ($p<0.0001$) and to have low birthweight sons ($p=0.02$) (Table 1). No other significant differences were observed.

As previously reported (13), black mothers had significantly higher levels of estradiol ($p=0.05$) and testosterone ($p<0.01$) in first trimester samples, but had significantly lower estradiol/testosterone and estriol/testosterone ratios ($p=0.01$). In contrast, there was no difference in the first trimester estriol levels between the groups. In third trimester samples, testosterone levels were significantly higher ($p<0.01$) and the estradiol/testosterone ($p<0.01$) and estriol/testosterone ($p<0.001$) ratios were significantly lower among the black mothers.

The examination of associations between maternal characteristics and testosterone levels found that testosterone levels were significantly associated with weight, height, BMI and age of white mothers, but not black mothers (Table 2). Among white mothers, both first and third trimester testosterone levels significantly increased with increasing weight and BMI, and significantly decreased with increasing height. In addition, there was an inverse association between age and testosterone level, which was stronger in third ($p<0.02$), than in first trimester samples ($p=0.13$). In contrast, no maternal characteristics were associated with testosterone levels in black mothers.

No significant relationships were observed in either white or black mothers between maternal characteristics and first trimester levels of estradiol or estriol, or the ratios of estradiol/testosterone and estriol/testosterone (Table 2). Several significant differences were noted in third trimester samples, however. Among white mothers, estradiol levels significantly decreased with increasing height ($p=0.03$), while among black mothers, estriol levels significantly decreased with increasing weight ($p=0.01$) and BMI ($p=0.02$). The associations between estriol and weight, and estriol and BMI among black mothers significantly differed from those among white mothers ($p=0.01$). Among white mothers, higher estradiol/testosterone ratios were significantly associated with increasing age

($p=0.01$) while higher estriol/testosterone ratios were significantly associated with both increasing age ($p<0.01$) and height ($p<0.01$). Both associations with the estriol/testosterone ratio were significantly different between white and black mothers. Cigarette smoking was not associated with any hormone at any time in black or white mothers (Table 2).

An examination of neonatal characteristics and testosterone levels uncovered no associations (Table 3). Estradiol levels, however, were positively associated with birthweight and length, and negatively associated with gestational age in white sons. The associations with length and gestational age were much stronger in first (length $p=0.01$, gestational age $p<0.01$) than in third trimester samples (length $p=0.24$, gestational age $p=0.45$). Among black sons, estradiol levels were negatively associated with gestational age in both first ($p<0.01$) and third trimester ($p<0.01$) trimester samples.

Among black sons, estriol was positively associated with birthweight and length, and negatively associated with head circumference and gestational age (Table 3). All associations, except that with gestational age, were stronger in third trimester samples. In contrast, among white sons, estriol was not related to birthweight, length or head circumference and was only related to gestational age ($p<0.01$) in the first trimester sample.

Among white sons, the estradiol/testosterone ratio was negatively associated with gestational age in both first and third trimester samples, while it was positively associated with birth length only in first trimester samples (Table 3). Among black sons, the estradiol/testosterone ratio was significantly associated with birth length only in third trimester samples and with gestational age only in first trimester samples.

The ratio of estriol/testosterone was negatively associated with birth length, head circumference and gestational age among black sons (Table 3). The associations with head circumference ($p=0.04$) and birth length ($p=0.01$) were only significant in third trimester samples. Among white sons, the estriol/testosterone ratio was negatively related to gestational age in both first ($p=0.05$) and third ($p<0.01$) trimester samples.

In comparing the neonatal associations between the white and black sons, only the association between gestational age and estriol differed significantly in both first and third trimester samples (Table 3). The association between length and the estriol/testosterone ratio differed significantly between the two groups, but only in the third trimester samples.

Discussion

Stimulated by racial differences in cancer risk, several studies have compared hormone levels in black and white mothers (9, 13, 21). Findings of higher testosterone levels among black mothers led to the hypothesis that lower risk of TGCT among black men may be due to the higher maternal testosterone levels (21). Alternatively, several TGCT studies hypothesized that increased risks associated with factors such as hyperemesis gravidarum (22) and low birth order (15) may link higher maternal estrogen exposure to TGCT (17, 23). One shortcoming of the TGCT studies, however, is that they have almost exclusively enrolled white men. Thus, it has not been clear that the results can be extrapolated to non-white populations. The findings of the current study support this concern in that some of the examined associations between perinatal factors and hormone levels varied between the black and white participants.

Why the hormone associations would differ by ethnicity is not clear. As the black mothers had significantly higher testosterone levels overall (13), it is conceivable that the testosterone associations only became apparent in the lower range of the white mothers. The stronger estriol association with perinatal characteristics of the black participants is

somewhat more puzzling as the black and white mothers had similar estriol levels. Estriol is predominantly produced by the placenta from dehydroepiandrosterone sulfate (DHEAS) elaborated by the fetal adrenal glands (24). Among the black sons, the positive association between estriol and neonatal size (birthweight, length and head size) may suggest that larger fetuses produce more DHEAS for conversion to estriol. However, the maternal estriol levels of the black and white participants did not differ even though the birthweight of the black sons was significantly lower than that of the white sons. This result may indicate that black fetuses produce more estriol than white fetuses of the same size. Alternatively, it is possible that the placentae of the black fetuses are more efficient at converting DHEAS to estriol. Thus, the lower risk of TGCT among black men might be related to one or more of several features; 1) higher maternal testosterone levels, 2) lower estriol/testosterone ratios, 3) greater fetal capacity to produce DHEAS, and 4) greater placental capacity to synthesize estriol. The paucity of data on black men with TGCT, however, makes it difficult to examine these hypotheses.

Among white populations, a number of prior studies of hormone levels and perinatal characteristics have been conducted. The relationship between maternal body size and estrogen levels, in particular, has been the focus of a number of investigations. While one study (10) reported a positive association between weight and free estradiol levels, two studies reported negative associations between height and estriol levels (11, 15) and another study found no association between body size and estrogen levels (9). In one of the studies (15), a negative association between body size and estradiol was found in white, but not in Chinese mothers. Similarly, the current study found negative associations between height and estradiol levels in white mothers, and between weight and BMI and estriol levels in black mothers. Examinations of body size and testosterone levels have been fewer. However, the current studies' result linking weight in white mothers to testosterone level is comparable to at least one prior investigation (9). As several recent studies have suggested a reduced risk of TGCT associated with increased pre-pregnancy weight or BMI (23, 25, 26), the current findings are consistent with a protective effect of higher maternal testosterone levels on white sons.

Studies of maternal age and hormone levels have reported that mothers younger than 20 years have lower estrogen levels than other mothers (9, 27), while highest estrogen levels are found in mothers either between 20 and 24 years (28) or between 20 and 34 years (9). The current study's findings of no association between age and estrogen levels, however, are consistent with results of Kaijser et al. (7, 11). The lower testosterone levels in older white mothers in the present study are also consistent with the report of Troisi et al. (9). As the risk of TGCT has been reported to increase with increasing maternal age by some (25, 28, 29), the current data suggest that lower maternal testosterone levels may increase risk of TGCT among white sons.

Positive associations between maternal estriol, estradiol and estrone levels and birthweight have all been previously observed (7, 8). The findings of the current study, with associations between estradiol and birthweight in white sons, and estriol and birthweight in black sons, are consistent with these results. The relationship between maternal estrogen levels and birthweight is of particular interest as birthweight has been associated with TGCT risk in a number of studies. The majority of the studies have found that low birthweight is associated with increased risk of TGCT (17, 23, 25, 28, 30-32). Several studies (16, 25, 32), however, reported a U-shaped relationship with risk, while several others (26, 33, 34) have reported no association. The combined results may suggest that there is more than one pathway to develop TGCT: one associated with high birthweight and a second associated with low birthweight. The current results suggest that the low birthweight pathway would be characterized by lower maternal estradiol levels in white populations. Conversely, the high

birthweight pathway would be characterized by higher maternal estradiol levels. As the great majority of cryptorchism studies have reported an association between cryptorchism and low birthweight (35-38), another feature of the low birthweight/low estradiol pathway may be cryptorchism.

Inverse associations between gestational age and maternal estradiol levels were found in both the current study and in a prior multiethnic study (15), but not in a study of estradiol levels at term (9). Among studies that have examined the relationship between gestational age and TGCT risk, most have found an inverse association (16, 26, 28, 31, 32, 39). As higher estrogen levels in first trimester were associated with shorter gestational age in the current study, higher first trimester estrogen levels may, by extension, be associated with increased risk of TGCT in white men. Given the positive association between first trimester estradiol level and birthweight, however, the estradiol-gestational age association may simply be due to the fact that larger babies tend to have shorter gestational periods. It is also possible that the apparent association is due to errors in determining gestation age.

It has been previously speculated that cigarette smoking lowers the production rate or the levels of total pregnancy estrogens (40). Studies that have examined the association between estradiol excretion and maternal tobacco smoking, however, have reached inconsistent results with some suggesting a negative association (41, 42), and others suggesting no association (43, 44). As recent studies, and the current study, have found no association between smoking and maternal serum estrogen levels (7, 9), the smoking-estrogen relationship remains unclear. It should be noted, however, that similar to previous studies (44-48), the current study observed a negative association between birthweight and smoking ($\beta = -3.87$, $p = 0.05$), which suggests that the relationship is not mediated by estrogens.

The current study had several advantages as well as limitations. Major advantages include that the study was conducted prospectively, included blood samples only from mothers pregnant with male fetuses, and included mothers of more than one ethnic group. The evidence suggesting that maternal hormone levels may be affected by fetal sex (9, 45, 46) makes the second advantage critical to the ability to extrapolate results to TGCT studies. Another advantage, the relatively large sample size, permitted sufficient statistical power to study the associations separately in low (black) and high (white) risk populations for TGCT (47). In the current study, any possible confounding effect of parity or multiple-birth on hormone levels was also eliminated. One theoretical limitation of the study is that the hormone levels were measured on samples that had been stored for approximately 40 years. Steroid hormones, however, are fairly robust as demonstrated by previous studies of freeze/thaw cycles on serum levels in stored samples (49). In addition, the current study found levels equivalent to those reported in other studies examining newly drawn samples (48). Finally, caution should be exercised in interpreting the results as there were a sizeable number of comparisons analyzed.

In conclusion, the current study found that maternal hormone associations with perinatal characteristics varied, sometimes significantly, by ethnic group. This finding suggests that extrapolation of perinatal associations with TGCT risk should not be done across ethnic groups. The current study also suggests that, based on the relationships between maternal characteristics and hormone levels, lower maternal testosterone levels may increase risk of TGCT among white men. The implications for black men are not as clear, due to lack of data of the relationship between perinatal characteristics and risk of TGCT in that group. Inclusion of black men in future studies would be of great benefit in understanding the complex relationships between in utero hormone exposures and TGCT risk.

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Table 1
Distributions of maternal and neonatal characteristics in white and black participants

Characteristics	White (n=150)		Black (n=150)		P value
	N	%	N	%	
Birth weight (kg)					
<2.5	1	0.7	9	6.0	0.02
2.5-4.0	141	94.0	137	91.3	
>4.0	8	5.3	4	2.7	
Birth weight for gestational age					
SMGA ^a	15	10.0	17	11.3	0.71
Not SMGA	135	90.0	133	88.7	
Birth length (cm)					
<50	54	36.2	49	32.9	0.28
50-51	45	30.2	58	38.9	
>51	50	33.6	42	28.2	
Head circumference (cm)					
<34	45	30.2	59	39.6	0.07
34	36	24.2	41	27.5	
>34	68	45.6	49	32.9	
Gestational age (wks)					
<37	14	9.3	20	13.3	0.27
37	136	90.7	130	86.7	
Maternal age (yrs)					
<20	32	21.3	77	51.3	<0.0001
20-24	88	58.7	59	39.3	
>24	30	20.0	14	9.3	
Maternal height (cm)					
<160	37	24.7	48	32.0	0.09
160-165	65	43.3	47	31.3	
>165	48	32.0	55	36.7	
Pre-pregnancy weight (kg)					

Characteristics	White (n=150)		Black (n=150)		P value
	N	%	N	%	
<53.1	52	34.7	49	32.7	0.91
53.1-58.9	46	30.7	49	32.7	
>58.9	52	34.7	52	34.7	
Maternal smoking during pregnancy					
No	96	64.0	107	71.3	0.17
Yes	54	36.0	43	28.7	
Social economic index (tertile)					
I	10	6.7	85	58.2	<0.0001
II	57	38.3	43	29.5	
III	82	55.0	18	12.3	

^asmall for gestational age

Table 2

Associations between maternal characteristics and serum hormone concentrations among white and black mothers in first and third trimesters

Maternal characteristics [§] (per SD)	White Mothers			Black Mothers			Whites vs. Blacks		
	1st Trimester		3rd Trimester	1st Trimester		3rd Trimester	1st Trimester		3rd Trimester
	MC [§]	p-value [¶]	MC [§]	MC [§]	p-value [¶]	MC [§]	p-value [¶]	p-value [¶]	p-value [¶]
Testosterone (ng/ml)									
Pre-pregnancy weight	0.13	<0.01	0.12	0.02	0.12	0.30	0.04	0.82	0.91
Height	-0.12	<0.01	-0.17	<0.01	-0.11	0.33	0.14	0.46	0.91
BMI	0.13	<0.01	0.13	<0.01	0.12	0.25	0.03	0.88	0.99
Age	-0.06	0.13	-0.13	0.02	-0.04	0.72	-0.11	0.58	0.73
Smoking	-0.004	-0.89	0.02	0.61	-0.07	0.53	0.004	0.98	0.56
Estradiol (ng/ml)									
Pre-pregnancy weight	0.36	0.12	0.87	0.24	0.01	0.97	-1.04	0.22	0.21
Height	-0.27	0.27	-1.66	0.03	-0.26	0.19	-0.02	0.98	0.69
BMI	0.34	0.11	1.00	0.14	0.04	0.82	-0.80	0.32	0.29
Age	-0.16	0.51	-0.38	0.63	0.08	0.70	0.18	0.84	0.54
Smoking	-0.06	0.75	-0.19	0.77	-0.22	0.29	0.10	0.91	0.59
Estriol (ng/ml)									
Pre-pregnancy weight	0.12	0.51	0.42	0.32	-0.04	0.69	-1.43	0.01	0.50
Height	-0.15	0.43	-0.29	0.50	-0.06	0.56	0.27	0.63	0.87
BMI	0.12	0.46	0.42	0.28	-0.03	0.71	-1.26	0.02	0.41
Age	-0.11	0.55	0.61	0.17	0.02	0.86	-0.17	0.78	0.61
Smoking	-0.04	0.78	-0.26	0.48	-0.11	0.29	-0.13	0.83	0.71
Estradiol/testosterone									
Pre-pregnancy weight	0.15	0.46	-0.53	0.41	-0.07	0.63	-0.04	0.94	0.27
Height	0.01	0.97	0.94	0.16	-0.04	0.78	-0.57	0.29	0.62
BMI	0.12	0.51	-0.60	0.32	-0.06	0.69	-0.10	0.85	0.38
Age	0.07	0.74	1.79	0.01	0.15	0.34	0.44	0.43	0.59
Smoking	-0.06	0.74	-0.13	0.82	-0.07	0.66	-0.14	0.80	0.91
Estriol/testosterone									
Pre-pregnancy weight	0.06	0.71	-0.41	0.37	-0.05	0.59	-0.31	0.49	0.57

Maternal characteristics [§] (per SD)	White Mothers				Black Mothers				Whites vs. Blacks			
	1st Trimester		3rd Trimester		1st Trimester		3rd Trimester		1st Trim		3rd Trim	
	MC [§]	p-value [¶]	MC [§]	p-value [¶]	MC [§]	p-value [¶]	MC [§]	p-value [¶]	p-value [¶]		p-value [¶]	
Height	-0.06	0.73	1.28	<0.01	0.001	0.99	-0.35	0.45	0.87		0.02	
BMI	0.06	0.68	-0.56	0.19	-0.04	0.59	-0.22	0.61	0.49		0.80	
Age	-0.01	0.96	2.45	<0.01	0.05	0.55	0.22	0.64	0.59		<0.01	
Smoking	-0.02	0.91	-0.27	0.50	-0.05	0.55	-0.22	0.65	0.76		0.85	

[§] Each maternal characteristic was rescaled by dividing its standard deviation which was calculated from the entire population

^{*} Mean change per standard deviation of each maternal characteristics.

[¶] Adjusted for gestational age of blood draw, maternal social economic index, and other maternal characteristics listed in this table.

Associations between neonatal characteristics and maternal serum hormone concentrations among white and black sons in first and third trimesters

Table 3

Hormone [§] (per SD)	White Mothers				Black Mothers				Whites vs. Blacks			
	1st Trimester		3rd Trimester		1st Trimester		3rd Trimester		1st Trim		3rd Trim	
	MC*	p-value [¶]	MC*	p-value [¶]	MC*	p-value [¶]	MC*	p-value [¶]	p-value [¶]	p-value [¶]	p-value [¶]	p-value [¶]
Testosterone												
Birth weight (grams)	54.02	0.48	75.44	0.37	-10.69	0.72	-7.36	0.80	0.29	0.29	0.38	0.38
Birth length (cms)	0.11	0.82	-0.15	0.78	-0.09	0.55	-0.24	0.13	0.54	0.54	0.89	0.89
Head circumference (cms)	-0.26	0.36	-0.02	0.95	-0.05	0.63	-0.11	0.23	0.63	0.63	0.67	0.67
Gestational age (weeks)	-0.39	0.36	0.56	0.20	0.001	0.99	-0.04	0.82	0.62	0.62	0.14	0.14
Estradiol												
Birth weight (grams)	83.60	<0.01	73.62	0.04	43.91	0.35	52.73	0.16	0.90	0.90	0.68	0.68
Birth length (cms)	0.46	0.01	0.26	0.24	-0.09	0.72	0.16	0.43	0.40	0.40	0.64	0.64
Head circumference (cms)	0.10	0.37	0.15	0.25	0.05	0.75	0.03	0.82	0.98	0.98	0.89	0.89
Gestational age (weeks)	-0.72	<0.01	-0.14	0.45	-1.09	<0.01	-0.42	0.03	0.10	0.10	0.29	0.29
Estriol												
Birth weight (grams)	41.45	0.09	73.63	0.07	19.90	0.75	117.72	<0.01	0.73	0.73	0.18	0.18
Birth length (cms)	0.18	0.23	0.21	0.42	0.05	0.87	0.43	0.04	0.70	0.70	0.14	0.14
Head circumference (cms)	0.05	0.57	0.16	0.27	-0.002	0.99	0.28	0.03	0.98	0.98	0.44	0.44
Gestational age (weeks)	-0.40	<0.01	-0.32	0.13	-1.54	<0.01	-1.00	<0.01	<0.01	<0.01	0.02	0.02
Total estradiol/total testosterone												
Birth weight (grams)	61.76	0.06	21.10	0.41	-15.47	0.78	19.25	0.60	0.72	0.72	0.51	0.51
Birth length (cms)	0.44	0.03	0.20	0.20	-0.14	0.64	0.43	0.02	0.40	0.40	0.14	0.14
Head circumference (cms)	0.22	0.08	0.13	0.17	-0.05	0.79	0.14	0.23	0.42	0.42	0.53	0.53
Gestational age (weeks)	-0.61	<0.01	-0.32	0.02	-0.79	<0.01	-0.26	0.18	0.60	0.60	0.47	0.47
Total estriol/total testosterone												
Birth weight (grams)	24.18	0.36	19.18	0.43	-47.65	0.47	35.78	0.22	0.56	0.56	0.22	0.22
Birth length (cms)	0.17	0.31	0.09	0.55	-0.07	0.84	0.39	0.01	0.89	0.89	0.03	0.03
Head circumference (cms)	0.08	0.44	0.12	0.17	-0.11	0.59	0.19	0.04	0.54	0.54	0.30	0.30
Gestational age (weeks)	-0.28	0.05	-0.37	<0.01	-0.93	<0.01	-0.39	<0.01	0.06	0.06	0.84	0.84

[§]Each hormone level was rescaled by dividing its standard deviation which was calculated separately for the first and third trimesters from the entire population.

* Mean change per standard deviation of each hormone

† Adjusted for gestational age at blood draw, maternal age at pregnancy, smoking during pregnancy, social economic index, maternal pre-pregnancy weight, maternal height, and gestational age (for birth weight, birth length and head circumference) and birth weight, birth length, head circumference (for gestational age).