Published in final edited form as:

Cancer Causes Control. 2018 August ; 29(8): 759–767. doi:10.1007/s10552-018-1054-8.

Racial differences in maternal and umbilical cord blood leukocyte telomere length and their correlations

Kari A. Weber, PhD¹, Christopher M. Heaphy, PhD^{2,7}, Corinne E. Joshi, PhD^{1,7}, Jiayun Lu, PhD¹, Sabine Rohrmann, PhD³, Jessica L. Bienstock, MD⁴, Tanya Agurs-Collins, PhD⁵, Alan K. Meeker, PhD^{2,6,7}, and Elizabeth A. Platz, ScD^{1,6,7}

¹Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Baltimore, MD 21205

²Department of Pathology, Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Baltimore, MD 21287

³Division of Chronic Disease Epidemiology; Epidemiology, Biostatistics and Prevention Institute; University of Zurich, Hirschengraben 84, 8001 Zürich

⁴Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, 600 N Wolfe St, Baltimore, MD 21287

⁵Division of Cancer Control and Population Sciences, National Cancer Institute, 9609 Medical Center Drive, Bethesda, MD 20892

⁶Department of Urology and the James Buchanan Brady Urological Institute, Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Baltimore, MD 21287

⁷Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, 401 N Broadway, Baltimore, MD 21287

Abstract

Purpose: Telomere length at birth sets the baseline for telomere shortening and may influence adult disease risk like cancer. Telomere length is heritable, but may also be a marker of exposures in utero, including those influencing racial differences in risk. We examined racial differences in telomere length in maternal and umbilical cord blood from male neonates, and maternal-neonate correlations to generate hypotheses.

Methods: Black and white pregnant women were recruited in 2006–2007 and followed to postpartum. Data came from questionnaires and medical records. Relative telomere length was measured by qPCR in leukocyte DNA. We estimated mean telomere length in mothers and

CORRESPONDING AUTHOR: Elizabeth A. Platz, ScD, Professor of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe Street, Room E6132, Baltimore, Maryland 21205, Phone: 410-614-9674, eplatz1@jhu.edu.

Compliance with Ethical Standards

Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

neonates (N=55 pairs) using linear regression and maternal-cord blood Spearman correlations, overall and by race.

Results: Black mothers had shorter age- and plate-adjusted telomere length (2.49, 95% CI 2.11–2.86) than whites (2.92, 95% CI 2.63–3.22; $P=0.1$) and black neonates had shorter telomere length (2.58, 95% CI 2.16–3.01) than whites (3.13, 95% CI 2.79–3.47; $p=0.1$), though not statistically significant. Differences were attenuated after further adjustment for maternal factors. Maternal-cord blood correlations were moderate ($r=0.53$, $p<0.0001$), and did not differ by race.

Conclusion: Telomere length may differ by race at birth due to both inherited and racial differences in maternal factors. This study was for hypothesis generation and results should be followed up in larger studies.

Keywords

telomeres; cord blood; race; maternal

Introduction

Telomere length at birth sets the baseline for the trajectory of lifetime telomere shortening. The length of a person's telomeres, repetitive sequences of DNA that protect the ends of chromosomes, may influence risk of adult diseases, including cancer. Telomeres shorten with cell replication and oxidative stress [1] and are shorter in peripheral blood leukocytes of older individuals [2], and in leukocytes of those exposed to modifiable factors such as smoking [3, 4], stress [5], and socioeconomic factors [6]. Racial differences in telomere length at birth [7–11] and in adulthood [11–14] have been explored in leukocytes and other tissues with differing results. Additionally, previous studies have reported that black individuals may experience accelerated shortening over time [7, 12]. However, contradictory results warrant further investigation.

Telomere length has also been shown to be highly heritable [15–18]. The mode of telomere length inheritance is still unclear [19] with some studies suggesting a stronger paternal influence [20, 21] and others, a stronger maternal influence [22, 23]. Beyond inheritance, maternal modifiable factors could also influence fetal telomere length, and the risk of disease later in life for the neonate. Supporting the utility of telomere length as a marker of the in utero environment, lower maternal folate intake and greater levels of maternal stress have been associated with shorter neonate telomere length in two recent studies [24, 25] and maternal exposure to higher levels of atmospheric particulate matter ($PM^{2.5}$) has been associated with shorter cord blood leukocyte and placental telomere length [26].

The current analysis examines perinatal exposures and racial differences in umbilical cord blood leukocyte telomere length. This analysis was made possible owing to a previous data collection effort developed specifically to study racial differences in blood factors in male neonates that may explain racial differences in later life prostate cancer risk [27, 28]. This was motivated by the substantially higher risk of prostate cancer incidence and mortality in black men compared to white men [29]. Indeed, of all of the common cancers in men, the

racial absolute and relative differences in the incidence and mortality rates is the highest in prostate cancer [29], and remain unexplained by standard cancer risk factors in mid-life.

We previously explored racial differences at birth in umbilical cord blood leukocyte telomere length in male neonates in this context [10] and we hypothesized that cord blood leukocyte telomere length would be shorter in black than white male neonates, reflecting both inherited differences by race and racial differences in prenatal exposures. We did not observe the hypothesized racial difference, but the pilot study had limited information on maternal and child factors that may differ by race and influence telomere length.

Thus, in the current, more comprehensive study in which we followed women throughout their pregnancy, we investigated racial differences in 1) leukocyte telomere length in maternal blood and cord blood of their male neonates, 2) correlations between maternal and cord blood telomere length, and 3) the associations of maternal factors with maternal telomere length and maternal and neonate factors with cord blood telomere length. The purpose of this work was to generate additional hypotheses regarding whether racial differences in telomere length at birth may account for some of the racial disparity in adult disease risk, such as cancer, especially prostate, and to inform whether these racial differences in telomere length are inherited, due to modifiable factors in utero, or both.

Methods

Study population

The Expanded Hormones in Umbilical Cord Blood Study (EHUB) is a longitudinal study of pregnant women designed to investigate racial differences in the hormonal and growth factor milieu in utero that may contribute to the racial disparity in prostate and breast cancers. Participants were aged 18 years or older, received prenatal care at the Johns Hopkins Outpatient Center, and delivered at the Johns Hopkins Hospital in Baltimore, MD, between 2006 and 2007. We recruited 185 women, either black or white, during the first 6–16 weeks of pregnancy and they provided consent. Women were eligible for EHUB if the father was the same race, they were willing to complete the study protocol, were not planning to bank their umbilical cord blood, had not been pregnant for 12 months prior to their current pregnancy, did not use in vitro fertilization or hormonal medications to become pregnant or to maintain their pregnancy, and did not have diabetes mellitus, thyroid disease, or polycystic ovarian syndrome.

Of the 185 recruited women, 126 completed the study. A participant was considered to have completed the study if she provided maternal blood during the first trimester, completed the questionnaire at the first prenatal obstetric clinic visit, completed the questionnaire at the first postpartum clinic visit, and umbilical cord blood was obtained at birth. For this study on racial differences in telomere length, neonates were eligible if they were a live, single birth, with no major birth defects, and full-term defined as the 37–42 weeks of gestation, and we restricted to male neonates. Of the 126, 59 neonates were full term, singleton males, and of these blood was located in the repository for all 59 mothers and 55 neonates, resulting in 55 maternal-neonate pairs (33 white, 22 black). EHUB and this analysis were approved by the Institutional Review Board of the Johns Hopkins Bloomberg School of Public Health.

Recruited women provided 15 mL of blood (sodium EDTA) at their first prenatal obstetric clinic visit (6–16 weeks) and completed a standardized questionnaire pertaining to pre-pregnancy administered by a trained research assistant. They were then asked for the dates of their future obstetrics appointments and permission to consult with the obstetrician about a potential due date so administration of study materials could coincide with these appointments. The second and third study visits coincided with their 20th (± 2) and 35th (± 1) week of pregnancy obstetrics clinic visits. At delivery, 15 mL of venous umbilical cord blood (sodium EDTA) were collected. Maternal and umbilical cord blood specimens were refrigerated until they could be processed, usually within 24 hours. The samples were centrifuged at room temperature for 15 minutes at 2,400 rpm, then separated into plasma, buffy coat, and red blood cells and aliquoted in cryovials and stored at -70°C . At the first postpartum obstetrics clinic visit, a research assistant administered a standardized questionnaire to the participants pertaining to their pregnancy. Pregnancy complications, weight, blood pressure, and urine glucose test were abstracted from medical records from each obstetric visit along with birth information, including birth weight and length and placental weight.

Assessment of maternal and neonate factors

Mother's age was assessed at time of enrollment. Pre-pregnancy maternal factors were obtained from the questionnaire administered at the first prenatal visit, and for the analysis categorized as follows: parity (0, 1, 2+), attained education (graduate degree, less than graduate degree), active smoking and secondhand smoke exposure history (exposed, not exposed), alcohol consumption history (ever drinker, never drinker), leisure time physical activity (hours/week), sedentary time (hours/week), pre-pregnancy weight, and height. We calculated body mass index (BMI) from weight (kg) and height (m) and categorized the women using the standard categories (normal 18.5 to $<25\text{ kg/m}^2$, overweight 25 to $<30\text{ kg/m}^2$, obese $\geq 30\text{ kg/m}^2$) [30]. The following pregnancy-related maternal factors were obtained from the questionnaire administered at the first post-partum clinic visit and expressed as follows: alcohol use during pregnancy (never drank, quit before pregnancy, quit during pregnancy), leisure time physical activity during each trimester (hours/week), and sedentary time (hours/week). The following maternal and neonate factors were obtained from the abstracted medical records: maternal weight recorded at the last obstetrics clinic visit before delivery, birth weight (g), placental weight (g), and birth length (in). Pregnancy weight gain was calculated by subtracting the weight recorded at the last obstetrics clinic visit before delivery from the self-reported usual pre-pregnancy weight. Neonate ponderal index (kg/m^3) was calculated from birth weight (kg) and length (m).

Measurement of telomere length

Leukocyte DNA was isolated from buffy coat from maternal blood and the cord blood of their neonates and re-purified to remove potential residual PCR inhibitors using the DNeasy Blood and Tissue kit (Qiagen, Venlo, Netherlands). Quantitative PCR was used to estimate the ratio of telomeric DNA to that of a single copy gene (β -globin) as previously described [31], with modifications [32]. Briefly, 5 ng of genomic DNA was used in a 25 μL volume for either the telomere or β -globin reactions; each sample was run in triplicate. Each 96-well plate contained a no template negative control and two separate 5-point standard curves

using a pooled leukocyte DNA sample; these standard curves allowed the PCR efficiency to be determined for each plate. Each plate also included three samples isolated from a series of cell lines with known telomere lengths, ranging from 3–15 kb, as determined independently by telomere terminal restriction fragment analysis. Inclusion of these samples provided an additional quality control check. Maternal-child pair samples were run on the same plate to limit plate-to-plate variation and the laboratory was blinded to sample identity. Samples were re-run if the coefficient of variation (CV) of either the telomere or the β -globin reaction was greater than 5% or either the telomere or the β -globin values fell outside the range of the standard curve. The mean telomere threshold (Ct) value and the β -globin Ct value were calculated from the telomere and the β -globin triplicate reactions, respectively. For those samples that were re-run (N=8), the mean telomere Ct and β -globin Ct values were compared to the original means to assess validity of the measurements. Because the re-run means were similar to the original run means, data from the original run were used (which preserves the benefit of running the maternal-cord blood pair samples on the same plate). Across all samples, the mean CV was 1.44% and 0.99% for the telomere and β -globin reactions, respectively. For each sample, the telomere measurement of the maternal or cord blood sample to the single copy gene (T/S) ratio (-dCt) was calculated by subtracting the β -globin Ct value from the telomere Ct value. The relative T/S ratio (-ddCt) was determined by subtracting the -dCt from a 5 ng sample in the cell line series from the -dCt of each unknown sample. These relative T/S ratios were used in the analysis (for simplicity called telomere length throughout). We also assessed plate-to-plate variation by comparison of the overall mean T/S ratio among the plates. Because we found evidence of plate-to-plate variation that was not due to differences in the characteristics of mothers and neonates among the plates, we adjusted for plate in the statistical analysis.

Statistical analysis

We calculated means, medians, and prevalences of maternal and neonate factors by race and compared them using a t-test (means), Wilcoxon-Mann-Whitney test (medians), or the Cochran-Armitage test (prevalences). Overall and separately by race, we calculated the mean or prevalence of maternal factors across tertiles of maternal telomere length and maternal and neonate factors across tertiles of cord blood telomere length, and tested for trend using Cuzick's non-parametric trend test or the Cochran-Armitage trend test (prevalences). Overall and separately by race, we estimated associations of maternal factors with maternal telomere length and maternal and neonate factors with cord blood telomere length using generalized linear regression adjusting for maternal age, and tested for heterogeneity using the likelihood ratio test. We confirmed the approximate normality of the T/S ratio distribution by the Shapiro-Wilk test.

We calculated mean maternal and cord blood leukocyte telomere length and 95% confidence intervals in whites and blacks using linear regression adjusting for maternal age and assay plate and additionally for maternal factors that differed by race, and tested for racial differences using the Wald test. Given the observed plate-to-plate variability in mean T/S ratio, we confirmed an absence of an interaction between race and assay plate using the likelihood ratio test. We calculated unadjusted and adjusted (partial) Spearman correlation coefficients to determine the correlation between maternal and cord blood leukocyte

telomere length overall and by race. All P-values are from two-sided tests. We considered $P < 0.05$ to be statistically significant. All analyses were done using SAS version 9.4.

Results

Table 1 shows maternal and male neonate factors by race. Black mothers were younger, less likely to have a graduate degree, were more likely to be overweight or obese, and less likely to be nulliparous than white mothers. Black and white mothers had different patterns of quitting the consumption of alcohol relative to timing of the current pregnancy. Black neonates tended to have lower birth length than white neonates.

Supplemental Table 1 and Supplemental Table 2 present non-parametric, unadjusted trends in maternal and neonate factors across tertiles of leukocyte telomere length in maternal blood and in cord blood, respectively, overall and by race. Maternal factors tended not to change across tertiles of maternal telomere length overall, except possibly for mean maternal age (inverse; P -trend=0.1), and few clear associations were observed within racial groups and when possibly present, they tended to be in one racial group only (Supplemental Table 1). Overall maternal and neonate factors tended not to change across tertiles of cord blood telomere length, except for mean pre-pregnancy BMI (inverse; P -trend=0.01), and for possibly the prevalence of a graduate degree (positive; P -trend=0.1; Supplemental Table 2). Few clear associations were observed with cord blood telomere length in either racial group and when present, they tended to be in one racial group and not the other.

Associations of maternal factors with maternal and cord blood telomere length, and maternal and neonate factors with cord blood telomere length estimated adjusting for age (except for the age association) and assuming linear relationships are shown in Tables 2 and 3, respectively, overall and by race. None of the maternal pre-pregnancy factors was associated with maternal telomere length, overall or by race, except possibly (all $P=0.1$) for maternal age (inverse), physical activity (positive), and nulliparity (inverse) in white mothers (Table 2). Overall, maternal education (positive; $P=0.09$), pre-pregnancy sedentary time (inverse; $P=0.1$), and pregnancy weight gain (inverse; $P=0.1$) were possibly associated with cord blood telomere length (Table 3). By race, the association between maternal education and cord blood telomere length was in the positive direction in both black and white ($P=0.09$) neonates albeit not statistically significant (Table 3). The association between sedentary time and cord blood telomere length was in the inverse direction for both black and white neonates, but was stronger and only statistically significant in black neonates ($P=0.02$). The association between placental weight and cord blood telomere length was in the positive direction in white neonates ($P=0.03$), but in the inverse direction and not statistically significant in black neonates (P -heterogeneity=0.05).

Racial differences in telomere length in the mothers and their neonates are presented in Table 4. Adjusting for assay plate and maternal age, black mothers appeared to have shorter mean telomere length (2.49, 95% CI 2.11–2.86) than white mothers (2.92, 95% CI 2.63–3.22), although this difference was not statistically significant ($P=0.1$). Further adjustment for maternal education and pre-pregnancy BMI, factors that most strongly differed by race, attenuated this racial difference ($P=0.3$). Adjusting for assay plate and maternal age, black

neonates appeared to have shorter mean cord blood telomere length (2.58, 95% CI 2.16–3.01) than white neonates (3.13, 95% CI 2.79–3.47), although this difference was not statistically significant ($P=0.1$). Further adjustment for maternal education and pre-pregnancy BMI attenuated this racial difference ($P=0.4$). Additionally adjusting for factors that were either associated with race or with cord blood telomere length did not further attenuate the racial difference (Table 4).

The Spearman correlation between maternal and cord blood telomere length was 0.53 overall ($P<0.0001$), and was similar (P -heterogeneity=0.6) in blacks ($r=0.60$) and whites ($r=0.49$). After adjusting for maternal age, and additionally individually adjusting for maternal factors and neonate factors, the correlation between maternal and cord blood telomere length did not substantially change overall or in whites or blacks (data not shown).

Discussion

In this study, we aimed to inform whether telomere length differences at birth could account for some of the racial disparity in adult disease risk. We observed that maternal age-adjusted leukocyte telomere length appeared to be shorter in both black mothers and their male neonate's cord blood than in white mothers and their male neonates' cord blood, although these differences were not statistically significant. However, these racial differences were attenuated after further adjusting for maternal education and pre-pregnancy BMI, factors that differed by race. We also found a moderately strong positive correlation between maternal and cord blood leukocyte telomere length, and this correlation was the same in blacks and whites. The positive correlation did not substantially change after further adjusting for maternal or neonate factors. Our results may add evidence to the hypothesis that telomere length in males differs by race at birth in part due to inherited differences and in part due to maternal factors that differ by race. These potential racial differences in telomere length at birth may help inform the racial disparity in risk of adult diseases such as prostate cancer, the initial motivation for this study.

Previous work by our group has observed shorter telomere length in prostate tissue of obese and physically inactive men [33]. Obesity has been associated with poorer prostate cancer outcomes, thus we hypothesized that telomere shortening may be a potential mechanism through which modifiable factors may influence prostate cancer risk [33]. Given this potential mechanism through which modifiable factors may influence prostate cancer risk, the racial differences we observed in some of these modifiable factors in utero and the potential result of shorter telomeres may be an additional mechanism.

Unlike our previous study in male neonates where we did not observe a difference between cord blood leukocyte telomere length in black and white male neonates [10], in the current study we did observe a suggestive racial difference (i.e., shorter telomere length in cord blood of black male neonates). Three previous studies investigated racial differences in newborn telomere length with conflicting results [7, 8, 34]. Okuda et al. ($n=134$) found no difference between black and white newborn cord blood leukocyte telomere length [34], whereas Drury et al. ($n=66$) and Rewak et al. ($n=143$) found that black neonates had significantly longer telomeres than white neonates [7, 8]. There are a few possible reasons

for the differences in findings among the five studies, including our current study. First, the five studies adjusted for differing arrays of potential confounders [7, 8, 10], if any [34]. Second, some studies included both male and female neonates combined [8, 34], while our previous and current study only included males [10]. Drury et al. reported that telomere length was different by sex and race, with the longest telomeres in black females [8], and Rewak et al. reported differences only among females after stratification by sex [7], whereas Okuda et al. included both sexes, but did not account for possible sex differences by race [34]. Third, the five studies used different methods to measure telomere length, which may have differing accuracies in detecting small differences in telomere length: four used qPCR [7, 8, 10] including the current study, and one used terminal restriction fragment (TRF) length analysis by Southern blotting [34]. Fourth, all of these studies, including both of ours, had small samples sizes, thus we cannot rule out chance as an explanation for the differences in findings among the five studies.

In our current study, we observed that, after age-adjustment, black mothers had suggestive shorter peripheral blood leukocyte telomere length than white mothers, but this difference was attenuated after further adjustment for education and BMI. These findings were similar to a study of placental telomere length that reported shorter telomeres in the placenta of black compared to white mothers, although the association remained after additional adjustment for maternal and infant factors [11]. Our current findings are in contrast to previous studies by Hunt et al. and Rewak et al. that found that black adult women had longer telomeres than white adult women [7, 12]. First, these three studies were conducted in populations with differing characteristics due to the different studies used such that the patterns of racial variation in telomere length could be different. Second, the studies took into account different potential confounders. For example, Hunt et al. had no measure of education [12], whereas we adjusted for education, which attenuated the racial difference.

Our finding of a positive correlation between maternal and cord blood telomere length overall is consistent with previous studies in healthy women in the UK [35] and in women with HIV [36], although the correlation we observed was stronger than in these two studies. Unlike the other studies, we accounted for additional maternal factors when calculating this correlation, and found that even after controlling for maternal and neonate factors, the positive correlation was not substantially changed overall, and there were no differences between blacks and whites. We conclude that racial differences in unadjusted cord blood telomere length are not explained by racial differences in the strength of the correlation between maternal and cord blood telomere length.

An additional aim of this study was to evaluate whether factors associated with maternal and cord blood telomere length differed by race, which we did using two approaches: calculated unadjusted means and prevalences of factors across tertiles of telomere length (did not assume linearity), and estimated age-adjusted associations between the factors and telomere length assuming linear associations. In general, few clear associations were observed for the factors investigated with maternal or cord blood telomere length in either racial group. When patterns of association were present they tended to be present in one racial group and not the other. Only for placental weight did the association statistically differ by race (positive

association with cord blood telomere length in white neonates, inverse association in black neonates).

Many aspects of this study merit discussion. With respect to strengths, this study used data and samples from a completed longitudinal study designed to evaluate racial differences in in utero biomarkers that may explain racial disparities in prostate cancer in adulthood. Because we conducted a longitudinal study in which we collected the mothers' blood each trimester, in the analysis of the correlation between maternal and cord blood telomere length we were able to use a blood sample from the first trimester when telomere length would be less influenced by the current pregnancy. Detailed data were available to characterize the mothers before and during pregnancy and their neonates at birth. In the current study, we implemented a thorough quality control protocol in the measurement of telomere length. The technicians running the telomere assay were blinded to race and to maternal or cord blood status. Maternal-neonate pairs were run on the same assay plate to avoid plate-to-plate variability between maternal and corresponding neonate samples. Because we noted plate-to-plate differences in overall mean telomere length, we adjusted for plate in the analyses of racial differences in telomere length.

This study also has some possible limitations. First, we cannot rule out that our findings may have been affected by the fact that black adults are known to have a lower percentage of neutrophils (a type of granulocyte) than white adults [37]. Neutrophil turnover is greater than other types of leukocytes, and greater proliferation can result in shorter telomeres. At birth, the correlation between telomere length in granulocytes and leukocytes has been shown to be 0.97 [38], thus, racial differences in leukocyte subpopulations are unlikely to fully explain the racial differences in cord blood telomere length. We cannot rule out this explanation for the racial difference in leukocyte telomere length in the mothers, however. Second, while we collected blood and detailed information from the mothers, we did not recruit the fathers. Some previous studies on adult children and their parents have reported that paternal and offspring telomere lengths are positively correlated, and that offspring telomere length is associated with paternal age [20, 21]. Another study found an inverse association between paternal education and telomere length in their offspring [6]. Irrespective of paternal contribution, our findings support the hypothesis that maternal telomere length may influence offspring telomere length. Third, our sample size was small, which may have limited our ability to detect as statistically significant the size of the racial difference in telomere length that we observed in the mothers and their male neonates' cord blood, thus, these results should be interpreted with caution. While the sample sizes are not extremely different from other studies of this kind, the results warrant follow-up with a larger sample. Additionally, because information was not collected, we could not evaluate maternal folate intake, stress, or exposure to atmospheric particulate matter (i.e., PM^{2.5}), which have been reported to be associated with shorter neonate telomere length [24–26]. Finally, this study was conducted at a single academic obstetrics department and was limited to white and black maternal-neonate pairs only. While the white and black mothers recruited into this study differed notably in their characteristics, especially educational attainment, we took into account these differences in the evaluation of racial differences in telomere length. We are uncertain about the generalizability of the findings to other white and black populations with characteristics that differ from our study population.

In conclusion, maternal telomere length was associated with umbilical cord blood telomere length, an association that did not differ by race or after accounting for maternal or neonate factors. Our age-adjusted findings suggesting that black mothers and their male neonates both may have shorter leukocyte telomeres than whites appear to be contrary to our previous findings in cord blood [10]. However, after adjustment for maternal factors in the current study, the black-white differences in both maternal and cord blood leukocyte telomere length were attenuated. Taken together, our results may add evidence to the hypothesis that telomere length differs by race at birth in part due to inherited differences between black and white mothers and in part due to maternal factors that differ by race. While the final associations were non-significant and should be interpreted with caution, these findings may help inform the racial disparity in risk of adult diseases like cancer, including prostate.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments:

This work was supported by a National Cancer Institute Comprehensive Minority Institution/Cancer Center Partnership grant (U54 CA091409), and a National Cancer Institute Cancer Center Support grant (P30 CA006973). Dr. Weber was supported by a National Cancer Institute Institutional National Cancer Research Service Award (T32 CA0093140) and the Johns Hopkins Bloomberg School of Public Health Department of Epidemiology Doctoral Research Fund. Dr. Joshi was supported by the Prostate Cancer Foundation. The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Table 1.

Maternal and male neonate factors by race, Expanded HUB Study, 2006–2007

	Race^a		p^b
	White	Black	
No.	33	22	
Maternal Factors			
<i>Pre-Pregnancy</i>			
Age (years, mean)	31	26	0.003
Graduate degree (%)	75.8	18.2	<0.0001 ^c
BMI (%)			
Normal (18.5–24.9 kg/m ²)	87.9	45.5	
Overweight (25–29.9 kg/m ²)	9.1	18.2	0.0003 ^d
Obese (≥ 30 kg/m ²)	3.0	36.4	
Exposure to cigarette smoke, active or secondhand (%)	42.4	45.5	0.7 ^c
Ever drinker (%)	84.9	81.8	1.0 ^c
Sedentary time (hrs/week, median)	12.0	10.0	0.4 ^e
Physical activity (hrs/week, median)	5.0	5.0	0.6 ^e
Number of previous births (%)			
0	60.6	40.9	
1	30.3	36.4	0.1 ^d
2 or more	9.1	22.7	
<i>Pregnancy</i>			
Sedentary time (hrs/week, median)	10.0	11.3	0.8 ^e
Physical activity (hrs/week, median)			
1 st trimester	4.0	5.0	0.2 ^e
2 nd trimester	4.0	5.0	0.2 ^e
3 rd trimester	4.0	5.0	0.5 ^e
Alcohol use during pregnancy (%)			
Never drank	15.2	13.6	
Quit before pregnancy	39.4	68.2	0.1 ^d
Quit during pregnancy	45.5	13.6	
Overall weight gain (lbs, median)	34.0	33.0	0.8 ^e
Weight gain (lbs, median) by pre-pregnancy BMI			
Normal	32.0	32.0	0.6 ^e
Overweight/obese	43.5	38.5	0.7 ^e
Neonate Factors			
Birth weight (g, mean)	3537	3388	0.2

	Race^a		p^b
	White	Black	
Birth length (in, mean)	20.3	19.7	0.03 ^e
Ponderal index (kg/m ³ , mean)	25.8	26.8	0.3
Placental weight (g, mean)	729.0	687.2	0.3

^aRace was self-reported by the mother. Mother and father of child must have been of the same race to be eligible for the Expanded HUB Study.

^bT-test unless otherwise specified.

^cChi-squared or Fisher's exact test.

^dCochran-Armitage test.

^eWilcoxon-Mann-Whitney test.

Table 2.

Age-adjusted^a change in maternal peripheral blood leukocyte telomere length per change in status of (binary) or per unit change in (continuous) maternal pre-pregnancy^b factors by race, Expanded HUB Study, 2006–2007

	Overall	P	White	P	Black	P	P-heterogeneity ^c
Maternal Factors							
<i>Pre-pregnancy</i>							
Age (years)	−0.03	0.3	−0.07	0.1	−0.01	0.7	0.3
Graduate degree (yes vs. no)	0.05	0.9	−0.15	0.7	0.61	0.3	0.2
BMI (kg/m ²)	−0.03	0.2	−0.01	0.9	−0.04	0.2	0.8
Exposure to cigarette smoke (yes vs. no)	0.10	0.7	0.42	0.2	−0.41	0.4	0.2
Ever drank alcohol (yes vs. no)	−0.01	1.0	0.33	0.5	−0.55	0.4	0.3
Sedentary time (hrs/week)	0.005	0.8	0.02	0.5	−0.01	0.8	0.4
Physical activity (hrs/week)	0.01	0.5	0.04	0.1	−0.002	0.9	0.2
Nulliparous (yes vs. no)	−0.21	0.5	−0.54	0.1	0.40	0.5	0.3

^aChange per year of age is not adjusted.

^bPregnancy factors occurred after the first trimester blood sample collection, and thus associations with maternal leukocyte telomere length were not determined.

^cInteraction between race and each factor.

Table 3.

Age-adjusted^a change in umbilical cord blood leukocyte telomere length per change in status of (binary) or per unit change in (continuous) maternal and male neonate factors by race, Expanded HUB Study, 2006–2007

	Overall	P	White	Black	P	P-heterogeneity ^b
Maternal Factors						
<i>Pre-pregnancy</i>						
Age (years)	-0.03	0.3	-0.02	-0.04	0.3	0.7
Graduate degree (yes vs. no)	0.64	0.09	0.83	0.37	0.6	0.6
BMI (kg/m ²)	-0.02	0.4	-0.08	-0.01	0.8	0.4
Exposure to cigarette smoke (yes vs. no)	-0.18	0.5	0.13	-0.65	0.2	0.2
Ever drank alcohol (yes vs. /no)	-0.005	1.0	0.25	-0.44	0.5	0.4
Sedentary time (hrs/week)	-0.03	0.1	-0.01	-0.06	0.02	0.2
Physical activity (hrs/week)	0.006	0.7	0.02	0.001	0.9	0.7
Nulliparous (yes vs. no)	-0.05	0.9	0.05	-0.23	0.7	0.8
<i>Pregnancy</i>						
Overall weight gain (lbs)	-0.01	0.1	-0.008	-0.01	0.2	0.9
Sedentary time (hrs/week)	-0.0005	1.0	-0.001	-0.0005	1.0	0.9
Physical activity (hrs/week)	-0.02	0.6	-0.01	-0.02	0.6	0.9
Neonate Factors						
Birth weight (g)	0.00009	0.8	0.00003	0.0001	0.8	0.9
Birth length (in)	0.20	0.3	0.01	0.30	0.2	0.5
Ponderal index (kg/m ³)	-0.02	0.6	0.01	-0.06	0.4	0.4
Placental weight (g)	0.001	0.2	0.002	-0.002	0.4	0.05

^aChange per year of age is not adjusted.

^bInteraction between race and each factor.

Racial differences in mean maternal peripheral blood and male neonate umbilical cord blood leukocyte telomere length, Expanded HUB Study, 2006–2007

Table 4.

	Adjustment ^a	Telomere length									
		Maternal peripheral blood leukocytes					Umbilical cord blood leukocytes				
		White	95% CI	Black	95% CI	P	White	95% CI	Black	95% CI	P
No additional adjustment		2.83	(2.55, 3.12)	2.62	(2.26, 2.97)	0.3	3.09	(2.76, 3.41)	2.65	(2.25, 3.05)	0.1
Age		2.92	(2.63, 3.22)	2.49	(2.11, 2.86)	0.1	3.13	(2.79, 3.47)	2.58	(2.16, 3.01)	0.1
Age, education, pre-pregnancy BMI ^b		2.89	(2.56, 3.22)	2.54	(2.12, 2.97)	0.3	3.03	(2.65, 3.40)	2.72	(2.25, 3.20)	0.4
Age, education, pre-pregnancy BMI, and all 4 neonate factors ^c		2.95	(2.60, 3.30)	2.47	(2.02, 2.93)	0.1	3.03	(2.64, 3.43)	2.63	(2.13, 3.14)	0.3
Age, education, pre-pregnancy BMI, sedentary time, and physical activity		2.92	(2.58, 3.26)	2.50	(2.06, 2.95)	0.2	3.08	(2.71, 3.44)	2.65	(2.17, 3.12)	0.2
Age, education, pre-pregnancy BMI, and nulliparity		2.92	(2.59, 3.25)	2.51	(2.09, 2.94)	0.2	3.05	(2.67, 3.43)	2.70	(2.21, 3.18)	0.3
Age, education, pre-pregnancy BMI, overall weight gain		2.90	(2.57, 3.22)	2.54	(2.13, 2.96)	0.2	3.03	(2.65, 3.41)	2.72	(2.24, 3.20)	0.4
Age, education, pre-pregnancy BMI, exposure to cigarette smoking		2.90	(2.56, 3.23)	2.52	(2.08, 2.97)	0.2	3.02	(2.64, 3.40)	2.72	(2.23, 3.22)	0.4

^a All models adjusted for telomere length assay plate.

^b Additionally adjusted for maternal factors that differed between blacks and whites.

^c Neonate factors: birth weight (g), birth length (in), ponderal index (kg/m³) and placental weight (g)