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# The effect of intrauterine stress on leukocyte telomere length in newborns

**Alketa Stefa[1], Agaristi Lamprokostopoulou[1], Anna Kontogeorgou[2], Despina Briana[2], Ariadne Malamitsi-Puchner[2], Ourania Tsitsilonis[4], Sarantis Gagos[3], Evangelia Charmandari[1,5]**

*[1] Division of Endocrinology and Metabolism, Biomedical Research Foundation of the Academy of Athens, Athens, Greece*
*[2] Department of Neonatology, Athens University Medical School, Aretaieion University Hospital, Athens, Greece*
*[3] Division of Genetics, Center of Experimental Medicine and Translational Research, Biomedical Research Foundation of the Academy of Athens, Athens, Greece*
*[4] Department of Animal and Human Physiology, Faculty of Biology, University of Athens, Athens, Greece*
*[5] Division of Endocrinology, Metabolism and Diabetes, First Department of Pediatrics, University of Athens Medical School, Aghia Sophia Children's Hospital, Athens, Greece*

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## Background

Telomeres are specialized nucleoprotein structures located at the ends of chromosomes playing a crucial role in genomic stability. They consist of tandem repeats of the noncoding hexameric TTAGGG sequence (Figure 1). Telomere shortening has been associated with cardiovascular disease, hypertension, diabetes type 2, atherosclerosis, coronary heart disease and stroke, and has been proposed as a biomarker for natural ageing and a prognostic factor for age–associated diseases.

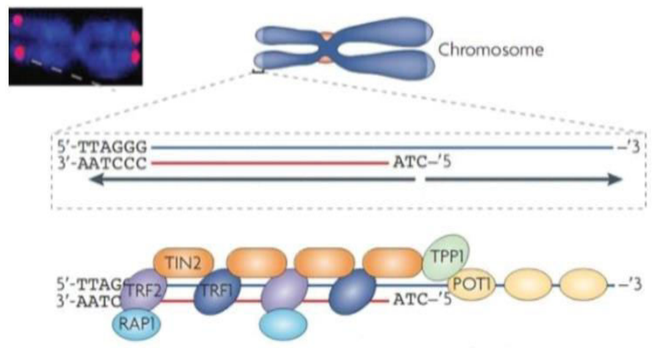


**Figure 1.** The overall structure of telomeres

## Objective and Hypotheses

The aim of the study was to determine whether decreased or increased intrauterine growth, representing stressful conditions, affects leukocyte telomere length (LTL) at birth.

## Patients & Methods

***Patients***: One hundred and fifty nine (n=159) full-term newborns participated in the study. Neonates were categorized as IUGR (intrauterine growth restriction) (n=18), LGA (large for gestational age) (n=12) or AGA (appropriate for gestational age) (n=129) based on their customized centiles at birth.

***Methods***: Cord blood was collected for DNA extraction, and LTL was determined by Multiple Monochrome Quantitative Real-Time PCR (MMQrtPCR) (Figure 2) and the Telomere Restriction Fragment assay (TRF) (Figure 3). The average LTL for each group of newborns was compared and correlated with selected anthropometric parameters of the newborns and the mother.

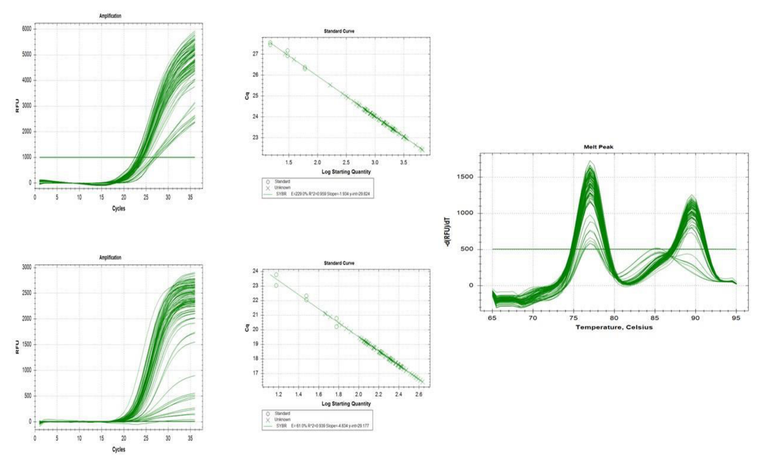


**Figure 2.** Multiple monochrome quantitative real-time PCR. In the figure are shown the standard and the amplification curves for the products of both telomeres and single copy gene.

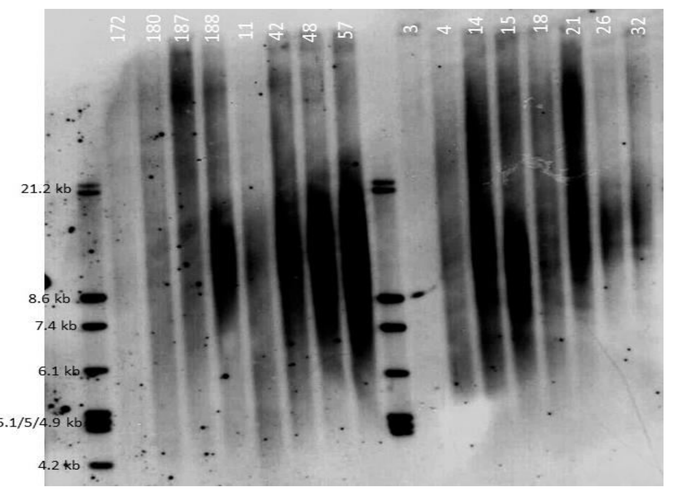


**Figure 3.** Telomere restriction fragment assay for IUGR (samples 172, 180, 187, 188, 11, 42, 48 and 57) and AGA (samples 3, 4, 14, 15, 18, 21, 26 and 32) newborns.

## Results

✓IUGR and LGA neonates did not have significantly shorter LTL compared with the AGA neonates. The results were analyzed by One-Way Analysis of Variance (Table 1, Figure 4).
✓There was no correlation between the LTL of the newborn and the mother's BMI and age.
✓Furthermore, no statistically significant difference in LTL between boys and girls was observed (Table 1, Figure 5).

**Table 1.**

| *Comparison between samples* | *Mean LTL ± SEM* | *P value* | *F value* | *R square* |
|---|---|---|---|---|
| *IUGR vs LGA vs AGA (TRF)* | *12.34 ± 0.46 vs 11.55 ± 0.42 vs 11.57 ± 0.48* | *0.46* | *0.77* | *0.02* |
| *IUGR vs LGA vs AGA (MMQrtPCR)* | *15.27 ± 4.47 vs 20.3 ± 7.58 vs 13.36 ± 2.93* | *0.96* | *0.03* | *0.001* |
| *Girls vs Boys* | *11.36 ± 0.69 vs 11.79 ± 0.68* | *0.66* | | |

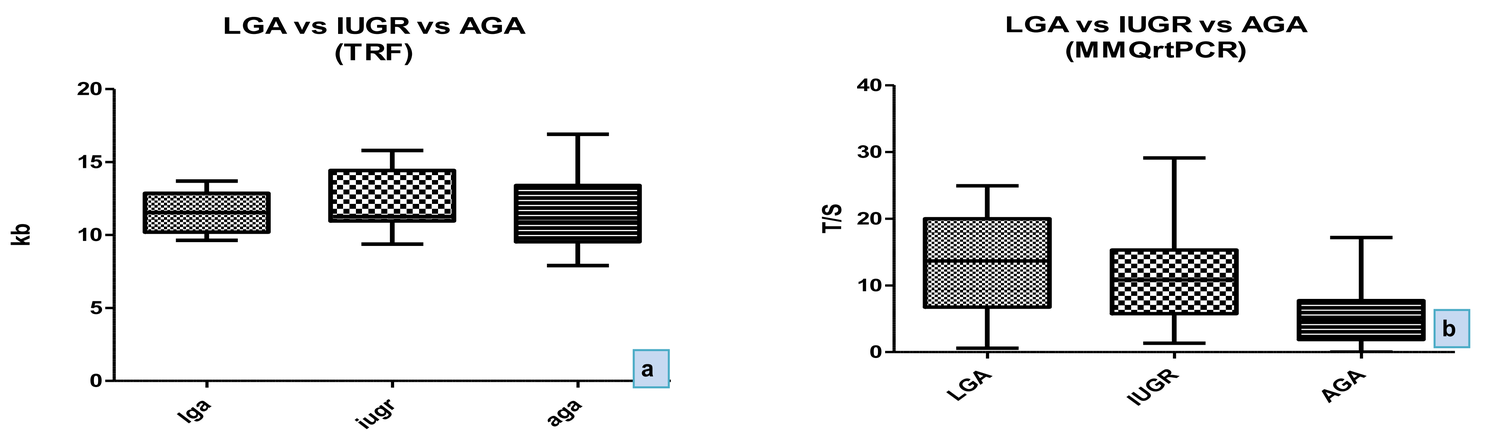


**Figure 4.** Comparison of the LTL between LGA, IUGR and AGA newborns as determined by TRF assay (diagram a) and MMQrtPCR assay (diagram b). No statistically significant difference was observed in both cases (ANOVA, *P*=NS).


**Figure 5.** Comparison of the LTL between boys and girls. No statistically significant difference was observed (t test unpaired, *P*=NS).

## Conclusions

✓IUGR and LGA neonates have similar LTL to that of AGA neonates.
✓The reduced LTL in various age – associated diseases is not seen at birth, but appears later in life, when most results of chronic conditions and exogenous stressors are observed.
✓Further studies using a larger sample size of IUGR, LGA and AGA newborns are required to confirm whether size at birth influences LTL.


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