http://jbcp.shahed.ac.ir 10.22070/JBCP.2022.16377.1159

Open Access Research Article

Journal of Basic and Clinical Pathophysiology
Print ISSN: 2322-1895, **Online ISSN:** 2345-4334
Vol. 10, No.1, June 2022

A Semiannual Publication of
Shahed University Press

Evaluation of leukocyte telomere length based on socioeconomic status in adults

Leila Nasiri[1], Mohammad-Reza Vaez-Mahdavi[2,3]*, Hossein Hassanpour[4], Nayere Askari[3,6] Sussan Kaboudanian Ardestani[3,5], Tooba Ghazanfari[3]

1. Department of Biology, Faculty of Basic Sciences, Shahed University, Tehran, Iran
2. Department of Physiology, Medical Faculty, Shahed University, Tehran, Iran
3. Immunoregulation Research Center, Shahed University, Tehran, Iran
4. Department of Gametes and Cloning, Research Institute of Animal Embryo Technology, Shahrekord University, Shahrekord, Iran
5. Institute of Biochemistry and Biophysics, Department of Biochemistry, University of Tehran, Tehran, Iran
6. Department of Biology, Faculty of Basic Sciences, Shahid Bahonar University of Kerman, Kerman, Iran

Abstract

Background and Objective: Understanding the social, economic, and physical determinants of telomere size is important to assess the risk of early biological aging. In this study, we investigated the association between socioeconomic parameters (marital status, income level, smoking status, and body mass index) and leukocyte telomere length (LTL) in Iranian adults. This cross-sectional study was part of a prospective cohort project in West Azerbaijan province, Iran.

Materials and Methods: One hundred and three adult participants (28-74 years) were included in this study. Personal and health data of each volunteer were obtained through the interview surveys, self-reports and clinical examinations. The LTL of each individual was relatively measured by real-time PCR. The association of relative LTL with socioeconomic status was evaluated after adjusting for age.

Results: The LTL was inversely correlated with the individual's age ($R=-0.226$, $P<0.001$). The age-adjusted LTL of participants was also positively associated with income level ($R=-0.301$, $P<0.001$) while it was not significantly correlated with overall marital, smoking, and body mass index (BMI) statuses. The age-adjusted LTL was increased in higher income levels compared to lower levels ($P<0.001$). There were no significant differences in the age-adjusted LTL between various variables of marital, smoking, and BMI statuses.

Conclusion: In the studied population, the income played a critical role in the telomere size and subsequent biological aging while smoking, marital, and BMI statuses did not have considerable influence on the telomere maintenance.

Keywords: Telomere length, Socioeconomic position, Biological aging

1. Introduction

Socioeconomic position (SEP) such as marital status, occupation, family income, smoking status, physical activity, education, and diet determines an individual's behavior and life/health conditions, and there is evidence that a weak SEP is concomitant with a progressive number and magnitude of long-act stressors (1, 2). It has been determined that the cumulative biological effect of being chronically exposed to social stressors, such as discrimination, racism, social class differences, unemployment, low income, alcohol consumption,

Revised: 19 May 2022, **Accepted:** 20 June 2022, **Available online:** 29 June 2022
Corresponding Author: Mohammad-Reza Vaez-Mahdavi **E-mail:** vaezmahdavi@shahed.ac.ir

and deficiency in the social support can extend the body's stress responses, which in turn elevates the risk of degenerative disease occurrence and exaggerate the aging process (3, 4). It has been reported that the socioeconomic differences have changed morbidity and mortality rates in different populations, and the higher prevalence of unhealthy behaviors in the lower SEP could worsen the health of individuals in the population and increase the morbidity and mortality (5). Combinations of social/physical parameters such as smoking, alcohol consumption, dietary patterns, physical activity, and body mass index have been responsible for 12% to 54% of the socioeconomic differences in mortality (5).

Telomeres are the repetitive sequences of DNA (TTAGGG) at the end of linear chromosomes that regulate the process of cell division and have been suggested as a biomarker of aging (6). In addition, telomeres act as molecular beacons for DNA damage to signal the cells for activation of the repair mechanisms or to signal senescence or cell death processes during the severe damage (7). Telomere shortening occurs rapidly during the first periods of life and continues with a slower process in the rest of life. This shortening process is influenced by a complexity of psychosocial, environmental, and behavioral parameters that accelerate it via the production of oxidative stress and inflammation leading to DNA damage (1). Previous studies have found that different markers leading to lower SEP may shorten leukocyte telomere length (LTL) (8,9). However, many studies have reported no correlation between SEP and LTL (1,10). For instance, previous studies that evaluated racism and ethnicity reported a longer LTL in blacks compared to whites (1,11). In the present study, we aimed to investigate the effect of many SEP parameters (i.e., marital status, income level, smoking status, and body mass index) on the leukocyte telomere length of volunteers from Rabat city (West Azerbaijan province, Iran). Many cities of West Azerbaijan province are deprived areas of Iran in terms of development indicators (12). Families of these cities are suffering from low income and unemployment as the greatest problem (13). No study has yet explored the relationship between SEP with LTL in this province. We hypothesized that many low SEP markers possibly reflect its effects on LTL in the people of this province.

2. Materials and Methods

2.1. Study design and sample preparation

The study was performed on one hundred and three adult volunteers (28-74 years) from Rabat city (a city in West Azerbaijan province, Iran). A blood sample was prepared from all participants. Also, personal data as SEP markers, i.e. smoking, marital, and income statuses were obtained through the interview surveys and volunteers' self-report. Clinical examinations were done by physicians to check out the health of participants and also estimate their body mass index (BMI). The SEP markers were evaluated in the following classification: 1) Marital status (single and married); 2) Smoking status (current smoker, smoked more than 100 cigarettes in their lifetime and smoked in the last 28 days and never smoker, smoked more than 100 cigarettes in their lifetime and did not currently smoke) (14); 3) Income (high, medium, and low); 4) Body mass index (BMI, kg/m2) (normal, BMI of 18.5–24.9; overweight, BMI of 25–29.9; obese, BMI of ≥30) (14). All data used in this study are related to the Sardasht-2 cohort project (code no. IR. Shahed. REC.1394.293).

2.2. DNA extraction and monochrome multiplex qPCR

The salting-out method was used to extract genomic DNA from whole blood samples. Extracted DNA was quantified by Nanodrop spectrophotometry. The samples with 260/280 absorbance ratios of more than1.8 were used for PCR. Relative LTL was measured using monochrome multiplex qPCR (MMqPCR) according to Cawthon (2009) (15) and Nasiri et al. (2021) (16). A specific kit (HOT FIREPol® EvaGreen® HRM Mix; Solis Biodyne, Korea) was applied to amplify DNA samples in triplicate by a real-time thermocycler (Rotor-Gene Q 6-plex, Qiagen, Germany). Telomere (T) and albumin (S) (as a single-copy gene) primers were synthesized according to Nasiri et al. (2021) (16). The melt curve of telomere and albumin was considered for the specificity of primers/amplicons and the absence of primer dimer formation. A standard curve was prepared from dilutions of a reference DNA (pooled from twelve controls). T and S are estimated according to this standard curve, then the relative TL was calculated for each sample through the determination of the T/S ratio.

2.3. Statistical analysis

Data were displayed as mean ± standard error (SE). The number of persons in various SEP markers was sufficient to compare statistically (Table 1). To compare relative LTL between different subgroups, values were adjusted to their ages. All data were checked for normality by Kolmogorov–Smirnov test (Table 1). The non-normally distributed subgroups were compared via non-parametric tests i.e., Kruskal-Wallis and Mann–Whitney. A Spearman correlation analysis was employed to assess the close relationship of age-adjusted telomere length with SEP markers. Also, the regression analysis between age and telomere length was presented as a graph. The P values less than 0.05 were noticed as statistical significant. The SPSS 26.0 software (IBM-SPSS, Inc, Chicago, IL, USA) was used for all mentioned statistical analyses.

Table 1. Telomere length distribution of social / physical subgroups

Total participants (n=103, 28-74 years)		
Subgroups	**Frequency** n (%)	**Homogeneity** P value
Marital status		
Single	5 (4.9)	0.048
Married	98 (95.1)	< 0.001
Smoking		
Never smoker	88 (85.4)	< 0.001
Current smoker	15 (14.6)	< 0.001
Body mass index (kg/m^2)		
Normal (18.5-24.9)	25 (24.3)	< 0.001
Overweight (25-29.9)	45 (43.7)	< 0.001
Obese (≥30)	33 (32.0)	0.007
Salary		
High	33 (32.1)	< 0.001
Medium	57 (55.3)	< 0.001
Low	13 (12.6)	0.053

P value greater than 0.05 indicates normal distribution of data in each subgroup (Kolmogorov–Smirnov test).

3. Results

Figure 1 shows the regression analysis between age and LTL. This graph confirmed a negative correlation between these two parameters (R=-0.226, P<0.001).

In table 2, the correlation of age-adjusted LTL with social/physical parameters was indicated. Only income level had a positive correlation with age-adjusted LTL (P<0.001) while smoking, marital and BMI statuses did not show any significant correlation with age-adjusted LTL (P>0.05).

In figure 2, the length of leukocyte telomere (after adjustment with age) was compared within the SEP subgroups. The age-adjusted LTL of participants in the high and medium income levels was greater than the low income level and also the age-adjusted LTL of the high income level was greater than the medium level of income (P<0.001). The participants with the married and single variables of marital status, non- and current smoking variables, and normal, overweight, and obese variables of BMI did not differ in the age-adjusted LTL (P>0.05).

Table 2. Correlation of age-adjusted telomere length with social / physical parameters

	Smoking	BMI	Marital	Salary
Correlation coefficient	0.045	-0.074	-0.139	0.301
P value	0.560	0.338	0.071	<0.001

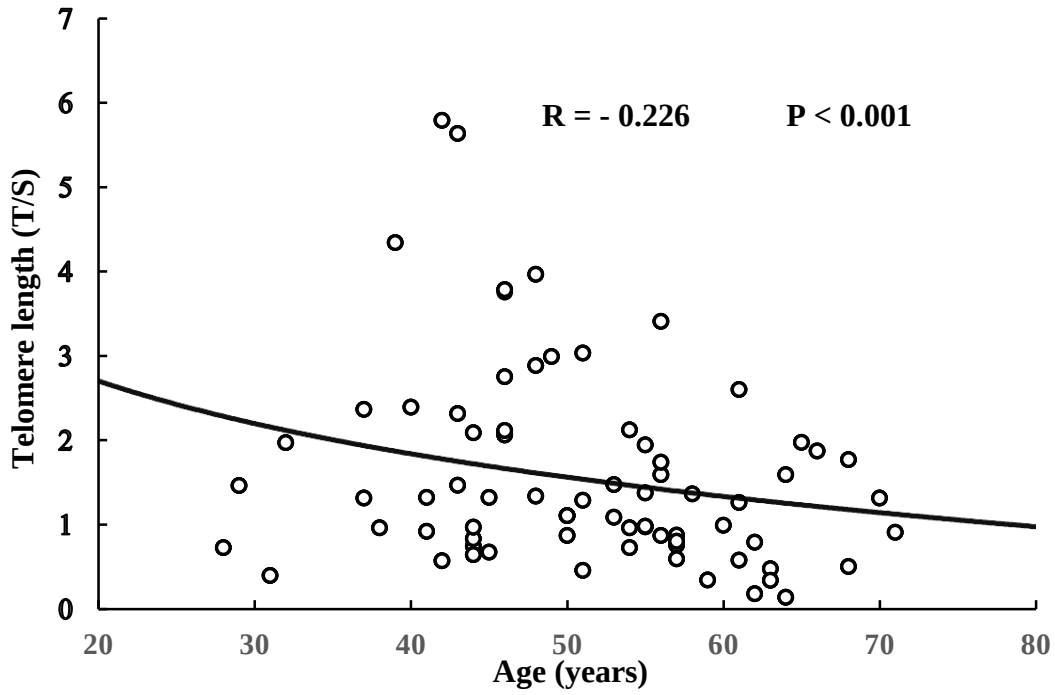

Fig 1. Graph of regression analysis between age and telomere length. T/S, telomere length/single copy gene.

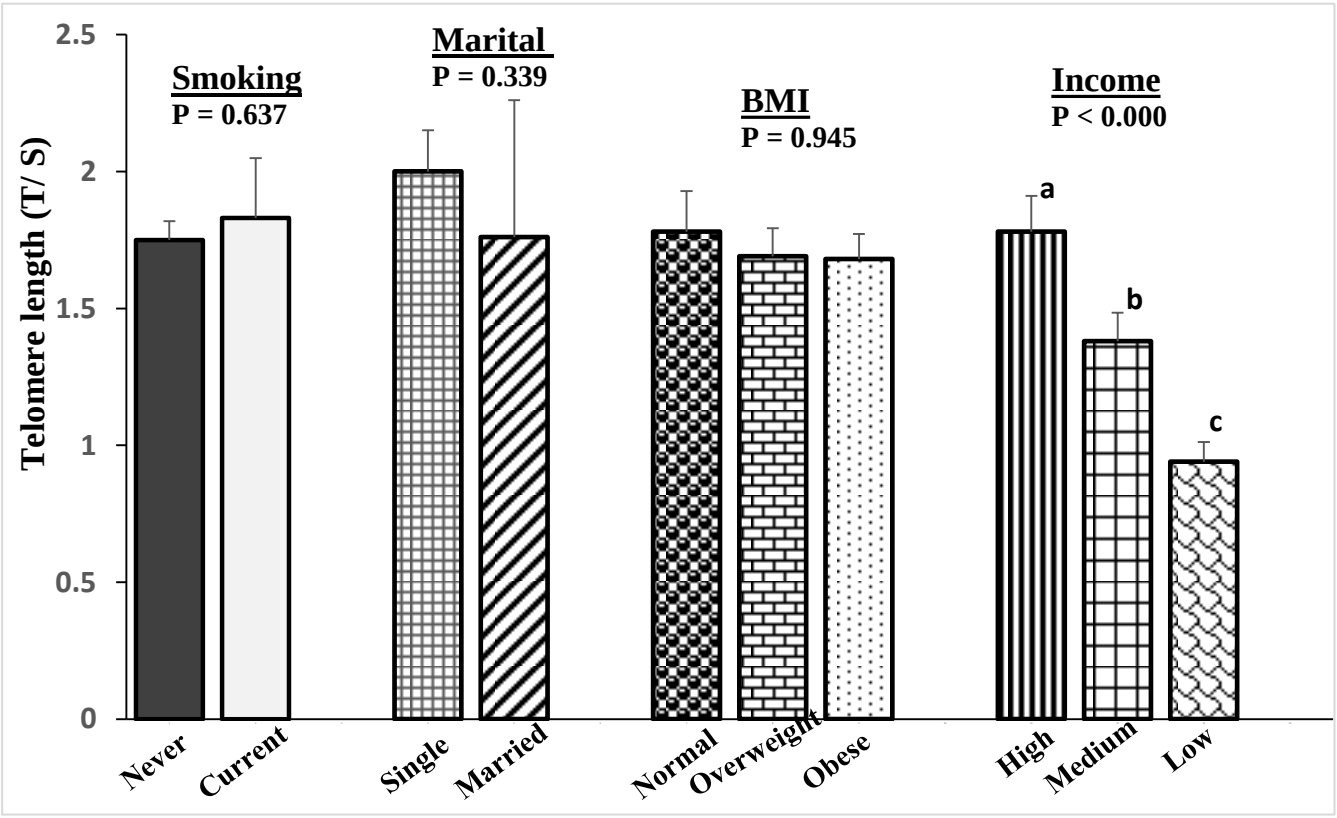

Fig 2. Comparison of leukocyte telomere length (after adjustment with age) within social / physical subgroups. a,b,c Significant difference between variables in each subgroup ($P < 0.05$).

4. Discussion

Telomere length has been confirmed to be maximum at birth and reduces progressively during the lifetime and thus could be an index of chronological aging (17). This age-related reduction in the length of telomere may be accelerated by various age-related diseases such as diabetes, hypertension, Alzheimer's disease, and cancer (18). Therefore, the attrition of telomere is important in determining both, the alteration in longevity and age-associated diseases in a person. It has been reported that aging and age-related diseases have a synergistic impact on the telomere size and also influence telomere length independently (17). However, in the present study, the inverse relationship between LTL and the age of healthy participants was confirmed statistically which is consistent with previous studies. Family low income and poverty are critical issues that influence individual health. Poverty is a strong factor in the accumulation of damaging childhood experiences and further injurious stress correlated with unpleasant health outputs in adulthood (19). Chae et al. (2014) evaluated racial discrimination as a stressor and noticed poverty as a confounder between discrimination and telomere length. Poverty was determined as the poverty ratio and the ratio of household income to the poverty threshold according to family members. They reported the high levels of unemployment in those families and confirmed that low income and poverty ratio were negatively associated with telomere length (20). Oliveira et al. (2016) also reviewed that there is evidence of a correlation between telomere size and poverty, indicating that poverty may promote telomere shortening through unknown mechanisms (21). Our data also indicated a direct association between income levels and LTL in the participants of Rabat city which is in agreement with the mentioned studies.

Overweight and obesity have been considered as chronic diseases and a common risk factor for higher morbidity and mortality that are associated with more production of oxidants. Oxidants can damage telomeres, and antioxidants can decelerate this damage (22). Müezzinler et al. (2014) reviewed that there is a negative relationship between levels of BMI and TL, but also reported a high variability between studies (23). Contrarily, Mundstock et al. (2015) in a systematic review and meta-analysis evaluated 63 original papers (including 119439 persons) and reported that 39 studies concluded either weak or moderate association between BMI and telomere length in addition to great heterogeneity (24). In the present study, there was no relationship between BMI levels and LTL. However, this inconsistency may explain that in addition to the overweight factor, other personal and environmental factors may also be needed to induce the adverse effect on the telomere size; and possibly different populations with various personal, social and environmental conditions show the different effects of overweight on the telomere length. Tobacco smoking is a defined health risk factor and exposure to adverse chemicals in cigarettes may promote oxidative stress and irrecoverable attrition to the telomere. Despite this biological impact, there have been disparities in the literature regarding association between telomere size and smoking. While a majority of studies reported no association between LTL and smoking (25), some findings indicated shorter telomeres with smoking (25, 26). Even, there is a report that smoking was leading to longer LTL (27). Of course, our data that showed a lack of relationship between smoking and LTL are agreed with most of the previous studies. However, the reason for the mentioned disparities is not determined and further investigations are needed.

The present findings showed no association between two variables of marital status (married and single) regarding LTL. Earlier studies reported conflicting data for this association. For instance, Mainous et al. (2011) determined that individuals married or living with a partner had a longer telomere, and those widowed, divorced, separated, or never married had shorter telomere in a model adjusted for age, gender, and race/ethnicity (28). Chen et al. (2020) also indicated that living singly, irrespective of the reason, was correlated with a shorter LTL and a higher risk of cardiovascular diseases (29). On the other hand, Petrovic et al. (2016) and Nasiri et al. (2022) reported contrary data (14, 30).

However, it seems that telomere length is influenced by a complexity of genetic, social, and environmental factors leading to biological aging; then it is perhaps that the evaluation of these factors individually does not offer accurate and reliable data. Therefore, it would be suggested that the concomitant effects of all these factors on LTL and also their interactions are evaluated in a unique system.

Conclusion

In the studied population of Rabat city, the income levels played a critical role in the telomere size and subsequent biological aging while smoking, marital, and BMI statuses did not have considerable influence on the telomere maintenance. It seems that family income is the most important factor in the health of people in this city.

Acknowledgment

The authors of the present study sincerely thank of Immunoregulation Research Center of Shahed University as well as Rabat people who volunteered to participate in this research.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding/Support
This research had been supported by the funds granted for the Sardasht-2 Iran Cohort study (code no.: (code no. IR. Shahed. REC.1394.293) via Vice Chancellor or Research of Shahed University.

Ethical approval
All procedures performed in this study involving human participants were in accordance with the ethical standards of the Ethics committee of the Board of Research of the Ministry of Health, and Shahed University (approved code: IR.SHAHED.REC.1399.151) 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.

References
1. Normando P, Bezerra F, Santana B, Calado R, Santos-Reboucas C, Epel E, et al. Association between socioeconomic markers and adult telomere length differs according to sex: Pro-Saúde study. Brazilian Journal of Medical and Biological Research 2020;53. https://doi.org/10.1590/1414-431X202010223
2. Nasiri L, Vaezmahdavi M, Ghazanfari T, Kaboudanian Ardestani S, Hassanpour H. Relationship of general health status (Goldberg method) with socioeconomic position and demographic features in Sardasht chemical veterans. Daneshvar Medicine 2022;29(6):1-13. https://doi.org/10.22070/DANESHMED.2021.15304.1137
3. Ribeiro AI, Amaro J, Lisi C, Fraga S. Neighborhood socioeconomic deprivation and allostatic load: A scoping review. International Journal of Environmental Research and Public Health 2018;15(6):1092. https://doi.org/10.3390/ijerph15061092
4. Vaez Mahdav MR, Nasiri L, Ghazanfari T. Evaluation of health and social inequalities in the occurrence of different types of chronic stress and their effect on immunoregulation. Immunoregulation 2021;4(1):3-16. https://doi.org/10.32598/IMMUNOREGULATION.4.1.4
5. Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, et al. Association of socioeconomic position with health behaviors and mortality. Jama 2010;303(12):1159-66. https://doi.org/10.1001/jama.2010.297
6. Srinivas N, Rachakonda S, Kumar R. Telomeres and telomere length: a general overview. Cancers 2020;12(3):558. https://doi.org/10.3390/cancers12030558
7. Verdun RE, Crabbe L, Haggblom C, Karlseder J. Functional human telomeres are recognized as DNA damage in G2 of the cell cycle. Molecular Cell 2005;20(4):551-61. https://doi.org/10.1016/j.molcel.2005.09.024
8. Huang Y, Yim OS, San Lai P, Yu R, Chew SH, Gwee X, et al. Successful aging, cognitive function, socioeconomic status, and leukocyte telomere length. Psychoneuroendocrinology 2019;103:180-7. https://doi.org/10.1016/j.psyneuen.2019.01.015
9. Cherkas LF, Aviv A, Valdes AM, Hunkin JL, Gardner JP, Surdulescu GL, et al. The effects of social status on biological aging as measured by white-blood-cell telomere length. Aging Cell 2006;5(5):361-5. https://doi.org/10.1111/j.1474-9726.2006.00222.x
10. Adams J, Martin-Ruiz C, Pearce MS, White M, Parker L, Von Zglinicki T. No association between socio-economic status and white blood cell telomere length. Aging Cell 2007;6(1):125-8. https://doi.org/10.1111/j.1474-9726.2006.00258.x
11. Needham BL, Adler N, Gregorich S, Rehkopf D, Lin J, Blackburn EH, et al. Socioeconomic status, health behavior, and leukocyte telomere length in the National Health and Nutrition Examination Survey, 1999–2002. Social Science & Medicine 2013;85:1-8. https://doi.org/10.1016/j.socscimed.2013.02.023
12. Feizizadeh B, Rezayi Bm, Hejazi Ma. Classification of socio-economic development levels in counties of west azerbaijan province, iran by gis and multi-criteria decision making. Geographic Space. 2013;12(40):1-25.
13. Mottaghi A, Amraie M, Ghorbani Sepehr A. An analysis of the causes of the tendency towards informal economy in border cities with emphasis on Coolbury employment (Case study: Sardasht city). Journal of Research & Urban Planning. 2022;12(47):271-286 https://doi.org/10.30495/JUPM.2022.4105
14. Nasiri L, Vaez-Mahdavi M-R, Hassanpour H, Askari N, Ardestani SK, Ghazanfari T. Concomitant use of relative telomere length, biological health score and physical/social statuses in the biological aging evaluation of mustard-chemical veterans. International Immunopharmacology 2022;109:108785. https://doi.org/10.1016/j.intimp.2022.108785
15. Cawthon RM. Telomere length measurement by a novel monochrome multiplex quantitative PCR method. Nucleic Acids Research

2009;37(3):e21-e. https://doi.org/10.1093/nar/gkn1027
16. Nasiri L, Vaez-Mahdavi M-R, Hassanpour H, Ardestani SK, Askari N. Sulfur mustard and biological ageing: A multisystem biological health score approach as an extension of the allostatic load in Sardasht chemical veterans. International Immunopharmacology 2021;101:108375. https://doi.org/10.1016/j.intimp.2021.108375
17. Rizvi S, Raza ST, Mahdi F. Telomere length variations in aging and age-related diseases. Current Aging Science 2014;7(3):161-7. https://doi.org/10.2174/1874609808666150122153151
18. Fasching CL. Telomere length measurement as a clinical biomarker of aging and disease. Critical Reviews in Clinical Laboratory Sciences 2018;55(7):443-65. https://doi.org/10.1001/jama.2010.297
19. Hughes M, Tucker W. Poverty as an adverse childhood experience. North Carolina Medical Journal 2018;79(2):124-6. https://doi.org/0.18043/ncm.79.2.124
20. Chae DH, Nuru-Jeter AM, Adler NE, Brody GH, Lin J, Blackburn EH, et al. Discrimination, racial bias, and telomere length in African-American men. American Journal of Preventive Medicine 2014;46(2):103-11. https://doi.org/10.1016/j.amepre.2013.10.020
21. Oliveira BS, Zunzunegui MV, Quinlan J, Fahmi H, Tu MT, Guerra RO. Systematic review of the association between chronic social stress and telomere length: A life course perspective. Ageing Research Reviews 2016;26:37-52. https://doi.org/10.1016/j.arr.2015.12.006
22. Zannolli R, Mohn A, Buoni S, Pietrobelli A, Messina M, Chiarelli F, et al. Telomere length and obesity. Acta Paediatrica 2008;97(7):952-4. https://doi.org/10.1111/j.1651-2227.2008.00783.x
23. Müezzinler A, Zaineddin A, Brenner H. Body mass index and leukocyte telomere length in adults: a systematic review and meta-analysis. Obesity Reviews 2014;15(3):192-201.
24. Mundstock E, Sarria EE, Zatti H, Mattos Louzada F, Kich Grun L, Herbert Jones M, et al. Effect of obesity on telomere length: systematic review and meta-analysis. Obesity 2015;23(11):2165-74. https://doi.org/10.1002/oby.21183
25. Astuti Y, Wardhana A, Watkins J, Wulaningsih W. Cigarette smoking and telomere length: a systematic review of 84 studies and meta-analysis. Environmental Research 2017;158:480-9. https://doi.org/10.1016/j.envres.2017.06.038
26. Révész D, Milaneschi Y, Verhoeven JE, Lin J, Penninx BW. Longitudinal associations between metabolic syndrome components and telomere shortening. The Journal of Clinical Endocrinology & Metabolism 2015;100(8):3050-9. https://doi.org/10.1210/JC.2015-1995
27. Baragetti A, Palmen J, Garlaschelli K, Grigore L, Pellegatta F, Tragni E, et al. Telomere shortening over 6 years is associated with increased subclinical carotid vascular damage and worse cardiovascular prognosis in the general population. Journal of Internal Medicine 2015;277(4):478-87. https://doi.org/10.1111/joim.12282
28. Mainous III AG, Everett CJ, Diaz VA, Baker R, Mangino M, Codd V, et al. Leukocyte telomere length and marital status among middle-aged adults. Age and Ageing 2011;40(1):73-8. https://doi.org/10.1093/ageing/afq118
29. Chen R, Zhan Y, Pedersen N, Fall K, Valdimarsdóttir UA, Hägg S, et al. Marital status, telomere length and cardiovascular disease risk in a Swedish prospective cohort. Heart 2020;106(4):267-72. https://doi.org/10.1136/heartjnl-2019-315629
30. Petrovic D, Pivin E, Ponte B, Dhayat N, Pruijm M, Ehret G, et al. Sociodemographic, behavioral and genetic determinants of allostatic load in a Swiss population-based study. Psychoneuroendocrinology2016;67:76-85. https://doi.org/10.1016/j.psyneuen.2016.02.003.