Biosaintifika 9 (2) (2017) 225-232

Biosaintifika
Journal of Biology & Biology Education

http://journal.unnes.ac.id/nju/index.php/biosaintifika

The Effect of Physical Activity agains the Telomere Length in the Leukocytes Cells of KONI Athletes

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DOI: 10.15294/biosaintifika.v9i2.6207

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History Article

Received 6 December 2016
Approved 8 June 2017
Published 17 August 2017

Keywords

physical exercise; telomere length; KONI; qPCR

Abstract

Telomeres are strands of non coding DNA at the ends of chromosomes that have the primary function to protect DNA from damage and maintain chromosomal stability. Physical exercise will increase the antioxidant activity can increase telomere proteins, lengthen telomeres and or protein networks associated with telomere so that the telomere remains long, or stopping telomere shortening. Telomere length was also associated with age. The purpose of the research was to determine telomere length of leukocyte cells in the KONI (Indonesian National Sports Committee) athletes in Jakarta. The research method is descriptive, by measuring telomere length using quantitative PCR on leukocyte cells. Samples are KONI athletes from several sports, including men and women athletes, with ages between 15-20 years. Used a control group (not athletes) is students of the Faculty of Medicine, University of YARSI. The results showed that there was no significant difference ($p > 0.05$) between telomere length group of athletes with the control group in both sexes. Similarly, telomere length between athlete male with female athletes also showed no significant difference ($p > 0.05$). It was concluded that physical exercise in athletes KONI at the age of 15- 20 years had no effect on telomere length in leukocytes. The results of this study provide information about the telomere length in Indonesian athletes at an early age.

How to Cite

Purwaningsih, E., Djannatun, T., Widayanti, E., Suciati, Y., & Zulhamidah, Y. (2017). The Effect of Physical Activity Agains the Telomere Length in the Leukocytes Cells of KONI Athletes. *Biosaintifika: Journal of Biology & Biology Education*, 9(2), 225-232.

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p-ISSN 2085-191X
e-ISSN 2338-7610

INTRODUCTION

Telomeres are the ends of chromosomes that are non-coding DNA replication in eukaryotic cells, which in humans is a replication of hexanucleotide TTAGGG. Hexanucleotide a core protein of the complex telomere shelterin and is associated with telomere function (Sabenroth et al., 2015) Cloning DNA strand can be done thoroughly with their typical structure of telomeres and the enzyme telomerase. If the cells do not have telomerase, the cells were not able to double-stranded telomere DNA. Thus causing DNA strand telomeres become shorter (Theimer & Feigon, 2006).

Telomere function is as a cover, which is essential for maintaining chromosome stability of recombination, fusion and degradation. Therefore, loss of telomere function might have had a great effect in the maintenance and integrity of chromosomes.

Telomere length can be used as an index of the biological age of a person or as biomarker of cell aging and can used to predict related incidence of morbidity and mortality (Laine et al., 2015). In addition to telomere length is often associated with the state of human health and at a certain age-related diseases in humans such as diseases related to the cardiovascular system (Hunt et al., 2008; Chen et al., 2011, Sabenroth et al., 2015)

Physical activity will increase the activity of antioxidant that can boost the protein telomere, extending telomeres and or tissue proteins associated with telomeres. Furthermore, physical activity can keep telomeres long stays or stop telomere shortening (Ludlow & Roth, 2011).

The research objective was to determine telomere length in KONI athletes leukocyte cells in some sports include men and women athletes. Benefits of the research is include the information about the length of telomeres athletes at a young age and become a reference for further research related to telomere length at the same age or different age.

METHODS

The study used a descriptive survey by measuring the telomere length on leukocyte cell of KONI athletes from several branches of sports. The research was conducted in the Laboratory Clinic Prodia and Integrity Laboratory YARSI University, Jakarta.

Subjects were students of SMP / SMA Ragunan, South Jakarta, about 40 people i.e. 20 men and 20 women. The controls are students of the Faculty of Medicine, University of YARSI totaled 38 people, including 17 men and 21 women). The age ranged from 15-20 years. The sampling technique is random sampling and differentiates the active individuals exercising with individuals who are not actively exercising. The sample criteria is aged 15 - 20 years,and healthy.Each subject of research conducted venous blood sampling as much as 5 cc, further isolation of lymphocytes and measurement of telomere length.

Samples were collected in tubes containing EDTA (Ethylene diamine tetra acid), then dilution with PBS solution (Phosphate Buffered Saline). Tubes labeled EDTA, then blood EDTA samples were rocked to prevent blood clotting. EDTA blood was transferred to a special tube and added a solution of PBS with comparing 1: 1. Mixture of blood EDTA (Ethylene diamine tetra Acid,) and PBS were transferred into tubes already containing Ficoll, then centrifuged at a speed of 400g, for 10 minutes. The middle layer (monocytes) were taken and transferred to a new tube, then added Ficoll and centrifuge back on the speed of 100g for 10 minutes. Centrifugation is done 2 times.

Measurement of telomere length were calculated using quantitative PCR (O'Collaghan et al., 2011), includes the step of DNA isolation, measuring the quality and quantity of DNA and genotyping. Measurement of relative elomere length is relatively proceed with the method Cawthon (2002).

DNA was extracted using the QIAamp DNA blood mini kit (Qiagen, Germany) according to the protocol indicated on the kit DNA is then stored in a freezer at -20°C.

The quality and quantity of DNA were analyzed using a spectrophotometer NanoDrop ND1000. This measurement is important to do in order to determine the concentration of DNA to be used in PCR and sequencing.

PCR (polymerase chain reaction) is a technique or method of reproduction (replication) enzymatic DNA without using organisms. With this technique, the DNA can be produced in large quantities at relatively short time so as to facilitate a variety of other techniques that use DNA. PCR was performed to determine the length of telomeres through repetition TTAGGG generated. Here is a primer sequence that was used to observe telomere length.

Telomere length data were analyzed by ANOVA followed by multiple comparison test using SPSS 20 version

Table 1. Oligomere used to measure the length of telomeres in human and rodent

	Oligomer Name	Species	Oligomer sequence (5'-3')	Amplicon size
Standards	Telomere standard	Human/ rodent	(TTAGGG)14	84 bp
	36B4 standard	Human	CAGCAAGTGGGAAGGTGTAATCCGTCTCCA-CAGACAAGGCCAGGACTCGTTTG TACCCGTTGAT-GATAGAATGGG	75 bp
PCR Primers	teloF	Human/ rodent	CGGTTTGTTTGGGTTTGGGTTTGGGTTTGGG TTTGGGTT	>76 bp
	teloR	Human/ rodent	GGCTTGCCTTACCCTTACCCTTACCC TTACCCTTACCCT	
	36B4F	Human	CAGCAAGTGGGAAGGTGTAATCC	75 bp
	36B4R	Human	CCCATTCTATCATCAACGGGTACAA	
	b-globinF	Human	GCTTCTGACACAACTGTGTTCACTAGC	82 bp
	b-globinR	Human	CACCAACTTCATCCACGTTCACC	
	36B4F	Rodent	ACTGGTCTAGGACCCGAGAAG	78 bp
	36B4R	Rodent	TCAATGGTGCCTCTGGAGATT	

(O'Collaghan et al., 2011),

This research has been getting Description Escaped Airworthiness Conduct of Research Ethics Committee, Research YARSI with No. 004 / KEP-UY / BIA / V / 2014 dated May 9, 2014

RESULTS AND DISCUSSION

Measurement of telomere length is done by creating a standard curve of telomeres compared to the standard curve Beta-globin with Quantitative PCR methods (O'Collaghan et al., 2011) and was followed by measuring the relative telomere length by calculating the ratio between telomere to single copy gene (T / S) Quantitative PCR method refers to a method of Cawthon (2002). The results of measurements of the relative telomere length of 38 samples are presented in Table 1. As supporting data presented data from anthropometric examination (Table 2, 3, and 4)

Statistical analysis with Levence test showed no difference between groups of athletes with the control group with a significance value of $p > 0.05$. By sex obtained telomere length between male athletes with female athletes did not show a difference with a significance value of $p > 0.05$).

Telomeres are nucleoprotein structures located at the ends of chromosomes of eukaryotic cells. Telomere length can be shortened with age and is involved in cellular aging. Therefore, the telomere length is a biomarker for aging (Mather et al., 2011). Telomeres consist of nucleotides TTAGGG replication. In humans, there is a repeat of 2000

Table 2. Relative telomere length value in athlete and control group leukocyte (ratio T / S)

Repetition	Athlete Group		Control Group	
	Male	Female	Male	Female
1	0.76	0.77	0.82	0.82
2	0.75	0.90	0.85	0.80
3	0.75	0.78	0.82	0.81
4	0.79	0.76	0.83	0.79
5	0.78	0.79	0.82	0.82
6	0.78	0.84	0.83	0.80
7	0.78	0.79	0.82	0.79
8	0.78	0.80	0.82	0.78
9	0.88	0.79	0.80	0.80
10	0.79	0.79	0.81	0.82
11	0.78	0.81	0.74	0.82
12	0.79	0.84	0.82	0.86
13	0.76	0.80	0.78	0.83
14	0.80	0.81	0.79	0.84
15	0.83	0.83	0.80	0.81
16	0.80	0.83	0.83	0.81
17	0.82	0.85	0.86	0.84
18	0.81	0.85		0.81
19	0.78	0.82		0.87
20	0.79	0.86		1.04
21				0.93
Mean	0.7900	0.8156	0.8141	0.8329
SD	0.02974	0.03456	0.02740	0.05789

In this study, the sample used is young people aged between 17-20 years, male and female gender, include athletes with some sports include athletics, football, volleyball, hangars, and boxing. Measurement of telomere length is taken from the cell leukocyte. The study by some researchers previously reported that telomere length at the individual has a different telomere length in different tissues or organs, such as the kidneys, liver, lungs or blood cells, lymphocyte cells have telomere length varied. Similarly, different species, length of telomeres is also different in different species (Cherif et al., 2003)

Various studies show that the influence of exercise to delay aging and prolong life. People who regularly exercise generally held steady despite the young age of aging. Compared with those who did not exercise, athletes runners had cells that looked much younger when observed under a microscope. According to Ludlow and Roth (2011), physical exercise will increase the activity of antioxidant that can boost the protein telomere, extending telomeres and or tissue proteins associated with telomeres. Sport / physical activity keep telomeres long stays or stop telomere shortening. Studies on 69 men and women volunteer aged 50-70 years showed that regular physical activity can maintain to the telomere length (Ludlow et al., 2008; Collin et al., 2003)

The results of this research showed that telomere length in KONI athletes leukocytes did not differ with the control group. This research was supported by previous studies reported that the leukocyte telomere length in cells of young

Table 3. Data of weight / height in a control and athlete group

Repetition	Athlete group				Control Group			
	Male		Female		Male		Female	
	Body Weight (kg)	Body height (cm)	Body Weight (kg)	Body height (cm)	Body Weight (kg)	Body height (cm)	Body Weight (kg)	Body height (cm)
1	60	170	47	158	91	187	39	155
2	53	156	49	167	83	169	46	152
3	68	168	46	158	66	175	52	157
4	58	162	82	172	70	165	56	156
5	59	165	68	167	56	160	50	161
6	62	168	60	169	160	160	58	157
7	64	169	46	155	69	172	61	163
8	74	185	44	158	62	165	44	149
9	60	165	46	150	110	176	49	159
10	55	167	69	169	51,5	170	42	158
11	54	174	62	165	77,5	171	61	158
12	67	176	55	163	96	165	61	155
13	54.5	176	58	170	80	173	55	153
14	53	163	71	154	87	174	51	155
15	57	170	77	172	66	166	60	153
16	66	178	60	174	67	178	46	161
17	62	168	72	175	87	184	49	159
18	60	164	46	155			49	158
19	61	171	50	168			58	163
20	50	163	48	161			60	160
21	45	154					60	163
Mean	59.40	168.19	57.80	164.00	81.12	171.18	52.71	157.38
SD	6.73	7.18	11.91	7.42	25.33	7.54	6.92	3.81

athletes with an average age of 20.6 years is not different from the control group, are volunteers who are not actively doing physical activity. Instead of continuous exercise in athletes older the average age of 51.6 years, showed that the telomeres are longer than those without exercise (Werner et al., 2008).

Another study on adolescent group Caucasians and African Americans ages 14 to 18 years also show telomere length (ratio T / S) does not difference compared to the control group. But the telomere length in Afrika.-American race is greater than Caucasians. It shows that the race can affect telomere length, whereas adipose tissue is not related to telomere length at this age. Physical activity causes the anti-aging effects are quite strong at a young age, particularly in women (Zhu et al., 2011)

Moderate physical exercise or aerobics, especially in women can maintain telomere length or increasing telomere length than those who are inactive. It is especially in women over the age of 40 years. Regular physical activity nothing to do with a decrease in oxidative stress and inflammation as well help prevent the onset of chronic diseases. It has been reported also that telomere length is influenced by various factors such as age, sex, race, smoking, physical activity, socioeconomic status, obesity, intake of multivitamins, alcohol consumption and hormone replacement therapy despite inconsistent findings (Enokido et al., 2014)

Relative telomere length (ratio T / S) at a young age (22-27 years) and elderly (66-77 years) between the group of athletes with non-athletes men have also been reported. At a young age, te-

Table 4. Waist circumference ratio data (LPI) cm) and Pelvic circumference (LPA) cm) data of athletes and the control group

Repetition	Athlete Group				Control Group			
	Male		Female		Male		Female	
	Wc	Pr	Wc	Pr	Wc	Pr	Wc	Pr
1	77	85	76	90	107	103	63	83
2	70	75	82	88	93	104	87	90
3	90	93	62	83	89	93	77	83
4	77	85	96	112	87	97	46	89
5	73	83	70	97	72	95	87.5	98
6	85	70	76	94	77	93	82,5	98
7	82	90	68	87	84	96	89	102
8	83	92	67	85	79	98	71	84
9	72	87	69	88	98	114	69	94
10	79	86	77	102	26	87	76	81
11	76	86	80	89	88	103	98	96
12	85	95	75	83	108	112	74	95
13	80	88	78	83	101	102	75	97
14	70	89	88	95	103	109	69	86
15	76	93	86	95	90	95	78	95
16	76	95	81	88	87	89	66	89
17	78	96	82	89	89,5	107	69	89
18	76	93	68	82			70	87
19	80	93	73	83			76	97
20	69	88	71	83			77	99
21	65	85					76	96
Mean	77.10	87.95	76.2 5	89.80	86.97	99.82	75.05	91.81
SD	6.05	6.47	8.23	7.61	18.69	7.80	10.76	6.18

Notes: Wc =waist circumference; Pr = pelvic ring

lomere length athletes are no different from non-athletes, while in old age, telomere length was significantly different. Group of athletes had longer telomeres than non-athletes (Osthus et al., 2012)

Results of a meta-analysis on the effect of physical activity on telomere length have also been reported. From a meta-analysis of randomized conducted 35 research results convering 41 329 samples reported that 20 the results showed no difference between telomere length group of athletes with the control group, while 15 other research showed significant differences (Mundstock et al., 2015).

In this study, telomere length between male athletes with female athletes is the same. There are no reports of previous studies related to telomere length among women athletes to male athletes. It has been reported that in male athletes . telomere length at a young age did not different from the control group and physical activity in athletes is not related to the relative telomere length in later life (Laine et al., 2015)

In individual non-athletes, researchers previously reported that telomere length between men and women did not differ significance. It is reported that telomere length-related changes with increasing age and male gender. There were no significant differences in telomere length between male and female. It was further reported also that socio-economic status, poor, diet and smoking habits may be associated with one's biological aging process. (Hunt et al., 2008; Shiels et al., 2011).

Things contradictions reported by other studies that found that newborn female babies had longer telomere than male babies. (Aubert et al., 2012). This is supported by other studies that also reported the difference in telomere length

Table 5. Thick fat data in athletes group and the control group

Repetition	Athlete Group						Control Group					
	Male			Female			Male			Female		
	Biceps	Triceps	S.Iliaca	Biceps	Triceps	S.Iliaca	Biceps	Triceps	S.Iliaca	Biceps	Triceps	S.Iliaca
1	6	5	4	5	7	9	6	9	14	6	11	17
2	5	4	6	5	6	6	10	14	20	7	9	11
3	4	4	5	6	8	8	5	7	7	4	6	11
4	5	6	16	10	14	15	11	14	18	6	9	14
5	5	5	7	10	14	15	11	12	14	8	13	13
6	5	5	5	7	14	10	5	11	12	9	28	18
7	6	5	5	6	9	8	6	11	16	6	8	10
8	4	6	5	6	9	7	5	8	12	10	13	16
9	5	4	6	6	11	10	7	22	26	9	13	15
10	5	6	6	6	12	9	3	4	6	6	9	8
11	2	5	6	5	5	10	5	9	18	6	9	18
12	6	5	6	4	5	5	12	19	28	12	18	19
13	5	6	5	5	4	5	8	6	15	10	19	17
14	4	6	6	9	9	10	7	12	13	8	14	13
15	5	6	6	5	5	10	5	8	10	9	11	15
16	6	10	7	3	5	5	4	7	6	5	12	11
17	4	8	6	5	6	5	8	15	19	6	9	13
18	4	6	5	3	5	5				6	8	15
19	5	5	5	4	5	5				11	15	21
20	5	5	6	3	5	5				4	10	15
21	4	6	6							11	16	16
Mean	4.76	5.62	6.14	5.65	7.90	8.10	6.94	11.06	14.94	7.57	12.38	14.57
SD	0.94	1.36	2.37	2.06	3.43	3.14	2.68	4.70	6.25	2.36	4.94	3.25

between both the sexes. It was reported that the white blood cells, women have longer telomeres than men (Nawrot et al., 2004; Barrett & Richardson, 2011, Gardner et al*.,* 2014; Dalgard et al*.,* 2015)

Physical activity spare time can increase telomere length of about 200 nucleotides in both men and women compared to inactive. Not reported differences in telomere length in male athletes and female athletes. Physical activity can be potentially as anti-aging. In addition to, intensive physical activity in men aged 20-30 years at least 10 years can extend the telomeres (Cherkas et al*.,* 2008; Sabenroth et al*.,* 2015).

Regular physical exercise can maintain telomere length, induces anti-aging, and has the effect of protective. Besides physical activity in men and women athlete with an average age of 20 years have anti-apoptotic effects on endothelial cells. Physical exercise will increase the activity of antioxidant that can boost the protein telomere, extending telomeres and or proteins associated with telomeres. Sport/physical activity keep telomeres long stays or stop telomere shortening. Studies on 69 volunteer men and women aged 50-70 years showed that regular physical activity to maintain telomere length (Ludlow et al., 2008; Ludlow & Roth, 2011; Werner et al., 2008)

In this study, the sample used is young people aged between 17-20 years, including male and female. Measurements taken from the telomere length of leukocyte cells in healthy individuals. A previous study reported that telomere length in individuals to variations, i.e. different organs have different telomere length, such as the kidneys, liver, lungs or blood cells, lymphocyte cells have telomere length varied. Similarly, different species, length of telomeres is also different (Cherif et al*.,* 2003).

Telomere length associated with a person's nutritional status. Assessment of nutritional status is calculated values between body weight and height person who is described as a person's body mass index. Overview nutritional status among athletes and non athletes depicted in Table 3.

Total fat content of a person's body is important to know because it determines whether a person can be classified as obese or not obese. Percentage of body fat in athletes and control group illustrated in Table 4 and 5.

Levels of body fat based on waist circumference and sex in athletes eligible men and women classified as normal because the percentage is greater than non-athletes in the same age group. Physical activity in athletes can prevent the accumulation of body fat (Azwar, 2004). A previous study reported that obesity is associated with increased oxidative stress, inflammation and telomere shortening is associated with increased body mass index and increased waist circumference and hip circumference, especially in women (Kim et al*.,* 2010)

The results of this study provide information about the telomere length in Indonesian athletes at an early age and provide information to the public about the effect of exercise on telomere length that can become the biomarker of the aging process.

CONCLUSIONS

Telomere length in KONI athletes in the 15-17 age equal to the length of telomeres with non athletes at the same age level. The length of telomeres in women athletes to male athletes are the same.

ACKNOWLEDGMENT

The author would like to thank the Directorate General of Higher Education through research funding Decentralization Higher Education Research Advancement on financial assistance for the implementation of this study and Laboratory Clinic Prodia for the assitanced in the procurement of reagents and facilities to conduct researsch

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