ORIGINAL ARTICLE

EXERCISE INDUCED RELEASE OF CREATINE KINASE IN NORMAL ADULTS

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Background: Creatine Kinase (CK) forms abundant ATP for muscular activity. High CK is an important indicator of muscle damage. The aim of this study was to evaluate the exercise induced changes in serum CK level in adults. **Method:** Two hundred healthy subjects in age range 18–24 years were selected. With their consent, demographic data was recorded and participants' 3 ml blood was drawn before exercise. Each was then subjected to run 3 Km on a Treadmill. Three millilitre blood was drawn after 4 hours of exercise for post-exercise serum CK level. Serum CK levels were run on a spectrophotometer using the reagent of CK-Nac (Spinreact®, Spain). Data were analysed on SPSS-20. **Results:** In females aged <20 years having BMI of 20.357±3.550 Kg/m^2 the mean pre- and post-exercise CK levels were 52.45±9.27 and 92.09±11.12 (U/L) respectively; and in females aged ≥20 years having BMI of 20.041±3.116 Kg/m^2 it was 52.33±7.73 (U/L) and 96.0±11.51 respectively. In males aged <20 years having BMI of 20.413±3.690 Kg/m^2, the mean pre- and post-exercising CK levels were 93.04±22.44 and 144.56±22.50 (U/L) respectively; and in males aged ≥20 years having BMI of 22.52±4.042 Kg/m^2, it was 104.03±20.34 and 147.27±18.70 (U/L) respectively. **Conclusion:** There were significant differences between pre- and post-exercise CK in two genders. The most profound factor which implements this change is age, gender and body mass index among the two age groups of both genders.

Keywords: Creatine Kinase (CK), Body Mass Index (BMI), Exercise, Treadmill
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INTRODUCTION

Creatine Kinase (CK) is an iso-enzyme, of about 82 KDa, found in the cytosol and mitochondria.[1] The two mitochondrial CK forms are ubiquitous and sarcomeric forms. While the three cytosolic CK forms are BB-CK (found in Brain cells), MB-CK (found in Cardiac cells) and MM-CK (found in the skeletal muscle tissue).[2] CK was first discovered by Lehmann.[3] The main physiological role ascribed to CK was thought to be the energy maintenance and homeostasis at sites of high energy revenue such as rapidly contracting skeletal muscle cells, since so long.[4] Despite of this function, the most important was to maintain constant levels of ATP and ADP, buffering the cell against rapid diminution of ATP.[5] The detection of the mitochondrial isozymes demonstrated that CK was located in different compartments and the conception of a creatine phosphocreatine shuttle was developed: a system power transmission between the local production of ATP (mitochondria) and the place of use (like, the myofibrils), where distinct isozymes are associated with sites of ATP production and consumption, acting as a transport mechanism for high energy phosphates.[6] Creatine kinase (CK) catalyses the reversible transfer of a phosphate group from phosphocreatine to ADP. This reaction is coupled to those catalysed by hexokinase (HK) and glucose-6-phosphate dehydrogenase (G6P-DH).

$$\text{Phosphocreatine+ADP} \xrightarrow{\text{CK}} \text{Creatine+ATP}$$

$$\text{ATP+Glucose} \xrightarrow{\text{HK}} \text{ADP+Glucose-6-phosphate}$$

$$\text{G6P+NADP}^{+} \xrightarrow{\text{G6P-DH}} \text{6-Phosphogluconate+NADPH+H}^{+}$$

The rate of NADPH formation, measured photometrically is proportional to the catalytic concentration of CK present in the sample.[7,8]

Skeletal muscles physiology reveals more detail concept of endurance activity which may increase or decrease accordingly to the exercise application. Tissue concentrations of phosphagens are related to maximum latent rates of ATP turnover and oxidative capacity. However, in the case of muscle fibres, this is associated with power output, phosphagen levels in burst muscles or in high level in faster exercise muscles, is typically higher than corresponding levels in muscles that exhibit more sustained modes of contractile activity.[9]

Due to exercise, either low intensity work done[10] or high intensity work done[11] muscular damage has been reported to occur at the level of the sarcolemma, Z discs, or both which is assessed by increase in blood serum CK levels because a high percentage of the body's CK is present in skeletal muscle tissue[12]. When acute damage occurs to the muscle cell structure, CK leaks into the interstitial fluid and is picked up by the lymphatic system.[13] The CK then travels through the lymphatic system and is eventually emptied back into the general blood circulation, which results in an increase in serum levels of CK.

MATERIAL AND METHODS

This comparative cross-sectional study was carried out in the Department of Physiology, Baqai Medical University from 15th Sep 2014 to 26th Feb 2015. The study included 200 adult healthy individuals having age ranging 18–24 years; 100 males and 100 females, who had no known morbidity. Written informed consent was obtained from every individual prior to the study.

Process of handling the treadmill (Model: SPR-OMA 8300) was demonstrated to the participant and they were asked to run for 3 Km. Participants were instructed to start walking on it with a slow speed of around 2 Km/hr for warm-up. Gradually the treadmill speed was increased up to 4 Km/hr for jogging, and then to 7 Km/hr for running.[14] Speed was adjusted according to participants' wish. As the participant finished the covered distance, treadmill was gradually stopped, and the participant was allowed to sit on a chair.

Total 6 ml of blood sample was obtained from every individual five minutes prior to exercise for the baseline estimation of serum creatine kinase, and 4 hours after exercise according to standard WHO Guidelines[15], in plain test tubes. Serum CK levels were measured using the kit CK-NAC SPINREACT® at 340 ηm on Spectrophotometer Model: NV 20, Henan Hi-Tech Instruments Co-Ltd. The demographic data was also recorded including age, height, and weight to calculate BMI. The data were analysed using SPSS-20. Paired sample *t*-test was used to compare the pre- and post-exercise levels of CK, and $p<0.05$ was considered significant.

RESULTS

In the age group <20 years there were 78 (39%) subjects, 23 males and 55 females; and in age group ≥20 years there were 122 (61%) subjects, 77 males and 45 females.

The mean height of males was 171.71 Cm, and it was 161.40 Cm in females. The mean weight of males was 64.76 Kg and mean weight of females was 52.79 Kg. Collectively the mean BMI was 22.04 Kg/m^2 in males and 20.22 Kg/m^2 in females.

Mean pre-exercise CK levels in females aged 18–24 years was 52.4 U/L (35–75 U/L). Mean CK level in post-exercise (after 4 hours of exercise) in females aged 18–24 years was 93.85 U/L (65–115 U/L). Both CK levels fall within the normal range ($p<0.01$).

Mean pre-exercise CK levels in males aged 18–24 years was 101.5 U/L (35–130 U/L). Mean CK levels post-exercise (after 4 hours of exercise) in males aged 18–24 years was 146.65 U/L (65–180 U/L). Both CK levels fall within the normal range ($p<0.01$).

Table-1: Pre- and post-exercise CK levels according to BMI in males

Age	Number	BMI (Kg/m^2)	CK (U/L)	
			Pre Exercise	Post Exercise
<20 Year	23	20.41±3.69	93.04±22.44	144.57±22.50
≥20 Year	77	22.53±4.04	104.03±20.34	147.27±18.70
$p<0.01$				

Table-2: Pre- and post-exercise CK levels according to BMI in females

Age	Number	BMI (Kg/m^2)	CK (U/L)	
			Pre Exercise	Post Exercise
<20 Year	55	20.36±3.55	52.45±9.27	92.09±11.12
≥20 Year	45	20.04±3.12	52.33±7.73	96.00±11.51
$p<0.01$				

DISCUSSION

In the present study, the correlation of serum CK with pre- and post-exercise were measured in healthy, untrained, non-athletic males and females with an age ranging 18–24 years. The serum CK level was measured before and after 4 hours of exercise.

The average reference BMI value of Pakistani males for 20–50 years of age has been reported as 21.95 Kg/m^2 and for females it was 21.20 Kg/m^2.[16] According to WHO standards, the BMI cut-off point for normal subjects of Asian population varies from 18.5 Kg/m^2 to 24.9 Kg/m^2.[17] In the present study, the average BMI values fall within the normal ranges of WHO standards.

The serum concentration of CK is an important indicator of skeletal muscle fibre damage in exercise[18], neuromuscular disease, muscle injury due to strenuous exercise and high fever, and systemic disorders like connective tissue disorders, renal failure, and viral infection[19]. During repeated and intense contraction of muscle, CK leaks from the skeletal muscle fibres into the plasma.[20] Therefore, the measurement of CK levels in pre- and post-exercise helps in diagnosis of some pathological conditions of the muscles.[21] The normal resting levels of CK for men ranges from 55–170 U/L while for females it ranges from 30–135 U/L.[22] CK level for males aged >18 years ranges from 52 to 336 U/L and for females aged >18 years it ranges from 38 to 176 U/L.[23]

One study on teenagers reported normal CK levels ranging from 36 to 102 U/L for girls and 55 to 584 U/L for boys.[24] Another study done on 10 young non-athlete students in Poland observed the CK levels before and after 2, 7, and 24 hours of exercise. After exercise the CK levels were found to be 160–185 U/L.[25] In our study the mean pre-exercise CK level in males aged <20 years was 93.04 U/L, and post-exercise it was 144.56 U/L. The mean pre-exercise CK level of females aged <20 years was 52.45 U/L, and post-exercise it was 92.09 U/L. Males have slightly lower CK level in post-exercise which is due to low body mass and due to moderate exercise. However, the CK level is higher in males than females which supports previous studies that

CK is more marked in males, blacks, untrained people, eccentric muscular contractions and downhill running.[26,27]

The mean CK levels vary with age, gender, race, muscle mass, physical activity and climatic conditions.[28] There is also a marked sex difference in normal resting CK levels, with young adult males having high serum CK level than young adult females.[28,29] It is accepted that the males have greater muscle mass than females with more muscle damage in males and shows high levels of CK after exercise.[30] Females have less muscle strength than males.[31,32] It is also reported that subjects with more than normal BMI have higher CK levels than those with normal BMI.[33,34]

In the present study, the pre-exercise CK level of females aged <20 years was 52.454 U/L, and in females aged ≥20 years the mean CK level was 52.33 U/L. The post-exercise CK levels in females aged <20 years was 92.09 U/L while in females aged ≥20 years the mean CK level was 96 U/L. This indicates that due to slightly more body mass in females aged <20 years the CK levels are slightly higher in the pre-exercising state. However in the post-exercise CK levels, the BMI is less. Our results of CK levels fall within the range of previous work.

In the present study, the pre-exercise CK levels of males aged <20 years was 93.04 U/L, in males aged ≥20 years the mean CK level was 104.03 U/L. The post-exercise CK levels in males aged <20 years was 144.57 U/L, while in males aged ≥20 years the mean CK level was 147.27 U/L. This indicates that due to more body mass in males the CK levels are higher in the post-exercise due to more CK release.[30] Our results of CK levels fall within the range of previous work.

In our study, the CK was higher in males than in females. This is in agreement with Wolf MR *et al*[35] who reported that males have significantly higher concentration of CK, and it is gender dependent. Oudman *et al*[36] found that serum CK is dependent on BMI whereas it is independent of age, sex and ethnicity. Neal *et al*[37] have reported that the African Americans have relatively higher serum CK compare to American White, Hispanic and South Asians. Furthermore, in the following research they have also evaluated age factor related to CK which has shown a little significant difference in men but little or no difference in females.

During strenuous exercise, particularly in an untrained individual, greater muscle tension is produced and CK is released due to muscle tissue injury and alteration in myocyte membrane permeability.[38] Moreover, free fatty acids are also less during exercise in an untrained individual. The muscle gets fatigued with sustained exercise. Metabolic production of the glycolytic pathway triggers the formation of lactic acid which leads to increased CK levels.[39]

CONCLUSION

Pre-exercise CK levels were reduced while post-exercise CK levels were higher in subjects. The most profound factor which implements this change is age, gender, and muscle mass of the groups. The CK levels are higher in subjects having greater BMI. However, there was a variation among the two groups of female subjects in the post-exercise CK levels.

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