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Effects of Coenzyme Q10 Level on Clinical Parameters in Cystic Fibrosis Patients

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Abstract

Background: Cystic Fibrosis (CF) is a hereditary autosomal recessive genetic disorder that can affect many organs including the lungs and the digestive system. We aimed to assess the effects of coenzyme Q10 level on clinical parameters in cystic fibrosis patients.

Materials and Methods

This cross-sectional study was performed on 40 patients (13 females and 19 males) with cystic fibrosis who were admitted in Masih Daneshvari Hospital in Tehran- Iran, in 2017. A researcher-made questionnaire was distributed among them, and then the height, weight and arm circumference of the patients were measured and also their serum Q10 levels were evaluated. Then, the pulmonary function was evaluated using a 6-minute respiration test and a spirometry test. Finally, their total scores were calculated based on Shwachman score.

Results: The age range of participants was from 6 to 27 years old. Anthropometric indices such as weight (p=0.02, r=-0.408), age (p=0.016, r=-0.422), height (p=0.002, r=-0.520), birth weight (p=0.0113, R=-0.286), and height at birth (p=0.037, r=-0.37) had a significant negative relationship with coenzyme Q10. There was relationship between anthropometric indices and spirometry tests, including the association of FEV1 (act) with weight (p=0.00), and arm circumference (p=0.00) which were determined.

Conclusion: According to the results, there was no direct relationship between muscle mass and Q10. Besides, the mean age of Q10 was greater than that of in age group of 9-16 years old, which can be considered for nutrition or childhood reserves for coenzyme Q10 production, which is decreased due to increasing age and lack of intake or loss of body power for the production of coenzyme Q10.

Key Words: Anthropometry, Coenzyme Q10, Cystic Fibrosis, Respiratory System.

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1- INTRODUCTION

In children with Cystic fibrosis chloride channels in the membranes of many organs do not function properly. The patient will have the disorder forever (1-3). The Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein is a single polypeptide chain that contains 1480 amino acids which is a cyclic adenosine monophosphate (AMP) regulator for chloride channel, and also a regulator for other ion channels. The most abundant gene change in the CFTR protein results in the absence of phenylalanine at position 508 (4). Reduction of absorption or malabsorption in these patients can lead to complicated problems such as decreasing the antioxidant capacity and consequently increasing oxidative stress within the lung tissue in particular. One of the defense mechanisms weakened in these patients is the mechanism of the glutathione peroxidase system which is selenium-dependent and reduces beta-carotene and vitamin E in red cells. Consequently, providing fat-soluble substances and anti-oxidants in these patients is necessary (5).

Coenzyme Q10, also known as ubiquinone, is a fat-soluble pseudo-vitamin that contains 10 isoprenyl units in its side chain. It is a key component of the mitochondrial respiratory chain which is responsible for the production and synthesis of adenosine triphosphate (6). With the highest rate (40-50%) of Coenzyme Q10, cofactor of aerobic respiration and cellular aerobic metabolism mitochondria plays a role in oxidative metabolism and cellular respiration (7). Coenzyme Q10 exists in the cell membrane. It is also found in lipophilic cell organelles and in the balance between oxidants and antioxidants. Q10 forms 60% of low-density lipoprotein (LDL), 25% of high-density lipoprotein (HDL), and 15% of other lipoproteins. Thus, there is a strong relationship between Q10 and LDL. Human can either synthesize Q10 within the body or receive it through a diet. In addition to the antioxidant role it acts as an essential electron carrier; besides, in the synthesis of adenosine triphosphate (ATP) in mitochondria it acts in all cells of body (6). Side effects of its deficiency include liver damage, muscle aches, memory loss, increased risk of cardiac arrhythmias and cancer. This coenzyme is found low-level in autosomal recessive mutation, oxidative stress associated with aging and cancer processes and treatment with statins, and many neurological disorders, diabetes, cancer, muscular and cardiovascular diseases (8, 9). On the other hand, studies have shown that the consumption of corticosteroids have increased the risk of decreasing coenzyme Q10 in patients with asthma and it has led to an increase of oxidation and antioxidant decrease in the body which has increased the severity of the disease; yet, it was one of the usual drugs they consumed (10).

Moreover, due to the possibility of Q10 deficiency in these patients that results in possible muscular disorders and lung function reduction, a 6-minute breath test is performed in these patients. In patients with cystic fibrosis, considering their multiple organ disorders and in order to determine the progress and prognosis the disease process, it is essential to diagnose and evaluate pulmonary function in order to determine the quality of life for these patients. On the other hand, spirometry is the most important measure of pulmonary status in patients with cystic fibrosis which provides good indicators for the pulmonary function of these patients. Besides, this test is useful for the diagnosis of airway obstruction in these patients. Since Coenzyme Q10 measurements in these patients should be compared with a functional index, this study compared the simultaneous 6-minute walk test and spirometry test in these patients and then compared the results with the amount of

coenzyme Q10 in these patients. Surveys have shown that there is a relationship between lack of insufficient nutrient intake and various factors (11-13). The present study aimed to assess the effects of coenzyme Q10 level on clinical parameters in cystic fibrosis patients.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional study was performed on patients with cystic fibrosis who were admitted to Masih Daneshvari Hospital in Tehran from January to September 2017.

2-2. Methods

At first, the consent letter of participating in study was signed by the patients or their parents. Secondly, a questionnaire was distributed among them, and then the height, weight and arm circumference of the patients were measured and also their serum Q10 levels were evaluated. Then, the pulmonary function was evaluated using a 6-minute respiration test and a spirometry test. Finally, their total scores were calculated based on Shwachman index and the results were published.

2-3. Measuring tools

Height: The height of participants was measured using Seca height gauge (0.5 cm precision) without shoes. *Weight*: The weight was measured using Seca weighing scale (100 g precision) with minimum clothing and no shoes. The Body mass index (*BMI*) was the weight (in kg) divided by the height squared (in cm). *Arm circumference*: To measure first, it was necessary to hold the arm in a hanging state without contraction. Then the spine of scapula had to be determined, and the mid scapular spine to the elbow hat to be measured. *Ultimately arm circumference* was measured using a standard meter with no elasticity. It was determined according to the standard normal (Z) tables. To measure coenzyme Q10 the Q10 ELISA kit (from Zellbio Gmbh, the German company) was used in the laboratory of National Research Institute of Tuberculosis and Lung Diseases and the results were reported. At the beginning of the study, the children went through blood sampling (clot) which was performed through the Angiocath IV catheter (about 3 ml) by the nurse in the presence of the child's parents. Blood samples were transmitted to the blood tubes and then transferred to the laboratory. During the transfer, blood tubes should not be upside down because clot lysis might happen and the test would be complicated.

After transferring the samples to the central laboratory of Masih Daneshvari Hospital, the serum was isolated from the clots and then stored at -20° C or -70° C until the completion of all samples. Then, about one hour before performing the test, sample was melted and mixed for 2 minutes. According to the kits application the sensitivity was 2.6 ng/ml based on manufacturer's claims. The method of using the kit is that at first the standard sample in the kit must be six times diluted to reach the standard level for testing. In order to show the accuracy of process a diagram was obtained according to the product's catalog and the results were reported.

The 6-minute walk test: The patient is asked to walk on a flat surface for 6 minutes during which the patient is connected to the pulse oximeter device. The patient traverses a 30-meter route in a round trip. Every minute, the examiner asks the patient about the condition and says how much time is left. At the end, the patient sits on the chair and his/her SpO2 and heart rate are measured. Afterwards, the total traveled distance is calculated. Finally, the results were reported. *Spirometry test*: In spirometry, lung volumes, capacities, and expiratory flow rates are measured. If these rates are lower

than expected, it indicates a pulmonary dysfunction. It is performed in both sitting and standing positions. In sitting position, the patient should be completely straight in a way that the soles should be firmly stuck to the ground. Sitting position is the most convenient and suitable condition for spirometry. Standing position is more suitable for pregnant female, obese people and children. Afterwards, it has to put the nose clip to prevent the air coming out of the nose during strong exhalation and then it has to place the mouthpiece in the mouth (so that the tongue is placed beneath and the lips surround it).

Shwachman-Kulczycki score is designed and implemented to assess the status of patients with cystic fibrosis. Based on the existing indicators and considering five items (including general activity, physical test, nutrition, chest X-ray and total score) the patients are classified into four categories of severe, fair, moderate, good, and excellent.

2-4. Data analysis

In this study the variables were abnormal according to the results of Shapiro test. Therefore, eight subjects who caused the abnormality of population were excluded and the study was performed with normal tests. Parametric tests (such as T-test and ANOVA) were used to analyze the data. Pearson correlation coefficient test was used to examine the relationship between mean serum coenzyme Q10 levels and spirometry test and 6-minute walk test in cystic fibrosis patients. Analysis of Variance (ANOVA) was used to compare the mean of Q10 in terms of family factors (parents' education, parents' job, number of children in family, which number is the subject in family, type of childbirth, family relevance of parents) in patients with cystic fibrosis. In order to determine the correlation coefficient between Q10 and growth parameters in the population, Pearson correlation coefficient was used and non-parametric equation of Spearman correlation coefficient was used as long as the test conditions were not met. P-value less than 0.05 were statistically significant.

2-5. Ethical consideration

Ethics approval was obtained from the Shahid Beheshti University of Medical Ethics Committee (IR.SBMU.NRITLD.REC.1394.217).

3- RESULTS

In the present study, 32 subjects participated of which 13 subjects were females and 19 subjects were males. The age of the participants was from 6 to 27 years old and the most populated group was the group of over 17 years. In terms of education, the group of secondary school and high school had the highest rate of participants. Most parents had orientation cycle degree (completing secondary school). Considering the occupation, most mothers were housewives and most fathers were self-employed. The mean Q10 in the female group was significantly higher than the male group (p=0.04), and it had significant difference in various age groups (p=0.041).

Besides, considering the post-hoc test statistic, it is seen that in the groups of less than 8 years and 9 to 16 years the mean Q10 had a significant difference; in other words, the under 8 years group had a mean Q10 higher than that of 9 to 16 years group. A significant difference was seen in education level of different groups (p=0.029). Given the post-hoc test statistic, there was a significant difference in the mean Q10 of pre-school and elementary group and the college group; in other words, subjects in pre-school and elementary school averagely had a higher Q10 than subjects in college. Height at birth in different groups had a significant difference (p=0.021).

Moreover, considering the post-hoc test statistic it is noted that in the groups of below 49 cm and over 52.76 cm, the mean Q10 had a significant difference; namely, patients with below 49 cm of height at birth averagely had a higher Q10 than those with height of over 52.76 cm. In both normal and abnormal groups the FEV1% had a significant difference (p=0.02). The mean Q10 in the normal group was significantly higher than in the abnormal group. Using ANOVA test it is seen that p=0.047. Therefore, the mean Q10 was significant (0.05). In various groups the total score had significant difference, but due to the lack of standard deviation in the excellent group it was impossible to define the difference among the groups by post-hoc test. In addition to that, Pearson Chi-square test showed that there was a negative and significant relationship between Q10 and age, weight, height, and height at birth. By increasing each of the mentioned indicators, the amount of coenzyme Q10 decreased.

Table-1: Correlation coefficient between coenzyme Q10 and respiratory function, anthropometric and demographic variables

Variables	Correlation coefficient	P-value
FEV1	-0.248	0.172
The number of family members	0.162	0.377
Age (m)	–0.422	0.016
Weight (gr)	–0.408	0.020
BMI	–0.225	0.216
Height (cm)	–0.520	0.002
Height at birth (cm)	–0.286	0.113
weight at birth (gr)	–0.370	0.037
Arm circumference	–0.317	0.077
age of disease diagnosis (m)	–0.073	0.691
FVC	–0.307	0.087
MEF 25-75	0.010	0.956
The whole distance in 6 minutes	0.157	0.408
FEV1/FVC	0.194	0.288

FEV1: Forced Expiratory Volume in 1 second; BMI: Body Mass Index; FVC: Forced Vital Capacity; MEF: Maximum Expiratory Flow; BMI: Body mass index.

4- DISCUSSION

In the study, there was a significant relationship between Q10 and weight (P=0.047), height (P=0.005), and height at birth (P=0.004) in a way that the higher the anthropometric indicators were, the more Q10 in the subjects was seen. Other study that measured Q10 with anthropometric indicators had different results. In the study of Jose Del Pozo-Cruz et al. in 2014 on elderly people, the Q10 was compared to BMI; and a negative relationship between body mass index and Q10 was found in both male and female subjects (r=-0.515, p=0.017, r=-0.0515)(14). The results of this study demonstrated that there was a significant difference between coenzyme Q10 in both sexes (0.02); besides, FEV (act) was 0.03 and FVC (act) was 0.048. Another study on the growth status of children with cystic fibrosis showed that there was no difference between the heights of children over 15 and normal subjects, but the difference was observed in less than 5 years children.

The difference was seen in both genders. Within four years, there is found a difference between the indicators of height and weight but in 3 to 6 years children with CF, the anthropometric indicators are in the normal range of NCHS charts (15). Yet, some studies confirmed that among the children with cystic fibrosis, the female subjects had smaller indicators of height and weight than the male subjects, but ideal body weight (IBW) had no difference in both groups, and also the size of arm circumference was similar in both groups and no significant difference was noted.

It is seen that there was a significant difference between Mid-Upper Arm Circumference (MUAC), and fat percentage among the girls, the boys, and the reference group. The study of Stapleton et al. expressed that the difference between the affected and non-affected groups was in growth and anthropometric indicators. They emphasized that there was a difference in BMI, but there was no difference in anthropometry. So it was likely that the difference in data and results was due to anthropometric measurement type (12).

Another study (13) also confirmed that diminution of height, weight, and body mass index were seen in children of 5 to 8 years, but the difference with normal group was not significant; however, no diminution was seen in children of 9 to 12 years and they were like normal subjects. But the age group of 13-16 years has shown a significant diminution which contradicted the above mentioned comments. The remarkable point is that in children of 9 to 12 years, fat intake energy and basic energy had negative relationship with BMI, while it was a direct relationship in children of 13 to 16 years. Another study confirmed that there was a negative relationship between birth weight and coenzyme Q10 levels (11). In pregnant female, several studies also emphasized that in the second and third trimesters of pregnancy, a direct relationship between Q10 and birth weight was observed due to weight gain of mother (16). In addition to that, various studies portrayed a decrease of coenzyme Q10 with the increase of age, and in youngsters it was higher than in adults. It could be attributed to the fact that the amount of muscles in youngsters was more than in the middle aged people (17). On the other hand, there has been a negative relationship between BMI and the overall 6-minute walk in normal and obese subjects. But there are some opponents of these outcomes, such as Pelegrino who has contradicted this theory. Moreover, negative relationship has also been found between obesity and 6-minute walk (18).

In some surveys on adults it was seen that this test had a direct relationship with age, height, and BMI, but it has not been associated with weight. It has also been reported that it was higher in males than in females, but no significant difference was observed (19). In addition to the relationship between 6-minute walk test and BMI, the relationships with age, sex, height, and weight were also observed elsewhere (20, 21). In Chronic obstructive pulmonary disease (COPD) patients, there was no relationship between 6-minute walk test and body mass index, and muscle mass (22, 23). Studies on patients with CF have also shown that there were various views on this point. In a study there was no relationship between age, gender, and body mass index; besides, it emphasized that even there was no significant relationship among healthy subjects (24).

However, another study remarked that the patient subjects had a weaker 6-minute walk test than healthy subjects. Furthermore, the test had relationship with age, weight, height in patients, but no relationship was noted in healthy subjects (25). However, in another study the relationship was only observed between body mass index and 6-minute walk test (26). As shown in the table 1, in the study

of coenzyme Q10 and pulmonary function indicators just a direct and significant relationship was found in FVC (act) indicator, and no relationship was seen in other indicators. In another perspective, it can be concluded that the body fat can affect spirometry, but there are different ideas about it. In a study, increase of fat caused the reduction of FEV1/FVC.

In another study, weight gain of normal subjects reduced FEV1/FVC. But another study contradicted these views (18). The relationship between BMI and FEV1 was also seen in people with cystic fibrosis, but FEV1 of patients in 2000 was less than in 1993 (27). Losing weight and reduction of height in over three years subjects has shown a decrease in FEV1, and the relationship between muscle mass and FVC was also confirmed; Weight-for-age (WFA) of 3 to 6 years children had a direct relationship with FEV1, and it has also been reported a relationship between sufficient weight and reduction of lung function (15). Several studies are also available in sexual differences. In patients with CF, there was no difference between the two genders in reducing FEV1 at the age of 6 to 12 year-old, and it was seen that the increase in BMI has a direct relationship with increasing FEV1 (28).

Another study depicted that the lung function status had no relationship with FEV1, FVC, and age, but a direct relationship between BMI and the two indices was confirmed. Moreover, the relationship between FEV1(%), and life expectancy was reported directly and significantly (29). Another study showed that the lung function in both genders was lower than the normal status, and it also emphasized that FEF (Forced Expiratory Flow)(%) in girls was similar to that of normal group; while in the other cases it was lower than the boys (12). In assessing pre-term children, in the initial assessment, no difference was seen between healthy and pre-term groups in the FVC, but FEF of pre-term children exhibited a significant reduction in comparison to healthy subjects. But this study showed that in the second year, the difference was associated with a sharp decline in pre-term children due to the muscle mass. This difference would reduce lung function in later years (30). In preterm children with chronic obstructive pulmonary disease (COPD), and other children, studies have shown that air activity had an intense relationship with birth weight, and reduction of FEF25-75 was seen in smoking mothers who experienced low birth weight. Children with Borderline Personality Disorder (BPD) had reduction of FEV1/FVC and FEV1 in comparison to pre-term healthy children. A direct relationship between low birth weight and FEV1, FVC was proved, but no relationship between FEV1/FVC and FEF25-75 has been observed.

In another trial, there was a significant difference between the spirometry test of 8.5 years old subjects and 14.2 years old subjects, but all the subjects had reduction of FEF25-75 (31). In COPD patients the relationship between weight and FEV1/FVC% as well as the relationship between BMI and FEV1% were reported; besides, a direct and significant relationship between MUAC and FEV1/FVC was seen (32). Studies on obese subjects also showed reduction of FEV1 in obese subjects. Each 10 kg of overweight respectively reduced 96 ml and 51 ml in the spirometry test of male and female. It has been also shown that body mass index of less than 21.3 caused an increase in FEV1, but weight gain and increased BMI reduced FVC (33).

In the study of Laguna et al. no relationship was found between Coenzyme Q10 and FEV% (34). In the present study, there was a direct and significant relationship between the 6-minute walk test and spirometry indicators such as FEV1 (act), FEV1 (%), FVC (act), FVC (%), and MEF25-75 (act).

Some studies have shown that there was a direct relationship between the 6-minute walk test and the FEV1/FV, FEF25-75 in obese subjects (18). A direct relationship between FEV1, FVC and the 6-minute walk test was also seen in COPD patients (35). However, some studies contradicted these views. They have expressed that there was no relationship between the 6-minute walk test and FEV1, but they have confirmed a direct relationship between the test and FVC (23). In another study, association with FEV1, FVC was confirmed, but the 6-minute walk test had no relationship with FEV1/FVC (22).

A similar relationship has been observed in patients with cystic fibrosis. In some studies a direct relationship between FEV1 and 6-minute walk test has been observed (24, 26). Some other studies have emphasized that FEV1 can be a predictor of 6-minute walk test in patients with cystic fibrosis (13, 25). In a study conducted among patients with cystic fibrosis, the mean score of Shwachman index was 79.25 ± 10.11, and in terms of clinical status 4 subjects were excellent, 29 subjects were good, 14 subjects were moderate, and 4 subjects were fair. No subject showed severe condition (25).

On the other hand, in a study carried out four years ago in the same center (Masih Daneshvari Hospital), the Shwachman index of CF patients was 13.83 ± 13.8, but no patient was in excellent condition, and no relationship between this index and mortality was found. Considering physical activity, 13% were below normal and 39.1% were more than normal. Physical test showed that 8.7% were lower than normal, and 17.4% were higher than normal. On the other hand, in nutritional status 47.8% were below the normal range, and 8.7% were higher than normal range. The chest X-ray of 4.3% of subjects was below the normal and the same trend was above the normal, but in the recent study these figures were significantly different. In general activity 92.5% showed severe activity, in physical test 75% were severe, nutritional status of 70% was in the moderate condition, chest X-ray of 57% were in moderate condition, and in final assessment and total score 60% were found severe. The results showed weak and low status of the population even in the same center over the past 4 years.

5- CONCLUSION

According to the results, the mean of coenzyme Q10 in females was higher than in males. The results rejected the theory that there was a direct relationship between coenzyme Q10 and increasing of muscle mass. Besides, the mean age of Q10 was higher than that of the group of 9 to 16 years. It could be considered for nutrition or childhood reserves for the production of coenzyme Q10 because it would be decreased by increasing the age, lack of its consumption, and loss of body power to produce it. Moreover, high levels of coenzyme Q10 in pre-school children and elementary students were seen. It seems that in the future study by using coenzyme Q10 supplementation over the time it can be determined whether coenzyme Q10 has a severe effect on anthropometric parameters and course of disease.

6- ABBREVIATION

CF: Cystic Fibrosis, FEV1: Forced Expiratory Volume in 1 second, BMI: Body Mass Index, FVC: Forced Vital Capacity, MEF: Maximum Expiratory Flow.

7- CONFLICT OF INTEREST: None.

8- REFERENCES

1. Assal J, Groop L. Definition, diagnosis and classification of diabetes mellitus and its complications. 1999.

2. O'Sullivan BP, Freedman SD. Cystic fibrosis. Lancet. 2009 May 30;373(9678):1891-904.

3. Hassanzad M, Orooji A, Valinejadi A, Velayati A. A fuzzy rule-based expert system for diagnosing cystic fibrosis. Electronic physician. 2017;9(12):5974-84.

4. Cecil RLF, Goldman L. Cecil textbook of medicine: W.B. Saunders; 2000.

5. Papas A, Papas K, Hopkins W, Clark W. Coenzyme Q10 treatment for cystic fibrosis. Google Patents; 2004.

6. Lee BJ, Tseng YF, Yen CH, Lin PT. Effects of coenzyme Q10 supplementation (300 mg/day) on antioxidation and anti-inflammation in coronary artery disease patients during statins therapy: a randomized, placebo-controlled trial. Nutr J. 2013;12(1):142.

7. Overvad K, Diamant B, Holm L, Holmer G, Mortensen S, Stender S. Coenzyme Q10 in health and disease. European Journal of Clinical Nutrition. 1999;53(10):764-70.

8. Oudshoorn JH, Lecluse AL, van den Berg R, Vaes WH, van der Laag J, Houwen RH. Decreased coenzyme Q10 concentration in plasma of children with cystic fibrosis. Journal of pediatric gastroenterology and nutrition. 2006;43(5):646-50.

9. Valinejadi A, Sadoughi F, Salehi M. Diabetes Knowledge Translation Status in Developing Countries: A Mixed Method Study Among Diabetes Researchers in Case of Iran. International journal of preventive medicine. 2016;7:33. PubMed PMID: 26955462.

10. Gvozdjakova A, Kucharska J, Bartkovjakova M, Gazdikova K, Gazdik FE. Coenzyme Q10 supplementation reduces corticosteroids dosage in patients with bronchial asthma. Biofactors. 2005;25(1-4):235-40.

11. Park E. Birth weight was negatively correlated with plasma ghrelin, insulin resistance, and coenzyme Q10 levels in overweight children. Nutrition research and practice. 2010;4(4):311-6.

12. Stapleton D, Kerr D, Gurrin L, Sherriff J, Sly P. Height and weight fail to detect early signs of malnutrition in children with cystic fibrosis. Journal of pediatric gastroenterology and nutrition. 2001;33(3):319-25.

13. White H, Wolfe SP, Foy J, Morton A, Conway SP, Brownlee KB. Nutritional intake and status in children with cystic fibrosis: does age matter? Journal of pediatric gastroenterology and nutrition. 2007;44(1):116-23.

14. Del Pozo-Cruz J, Rodríguez-Bies E, Navas-Enamorado I, Del Pozo-Cruz B, Navas P, López-Lluch G. Relationship between functional capacity and body mass index with plasma coenzyme Q 10 and oxidative damage in community-dwelling elderly-people. Experimental gerontology. 2014;52:46-54.

15. Milla CE. Association of nutritional status and pulmonary function in children with cystic fibrosis. Current opinion in pulmonary medicine. 2004;10(6):505-9.

16. Haruna M, Matsuzaki M, Ota E, Honda Y, Tanizaki T, Sekine K, et al. Positive correlation between maternal serum coenzyme Q10 levels and infant birth weight. Biofactors. 2010;36(4):312-8.

17. Crane FL. Biochemical functions of coenzyme Q10. Journal of the American College of Nutrition. 2001;20(6):591-8.

18. Gontijo PL, Lima TP, Costa TR, Reis EPd, Cardoso FPdF, Cavalcanti Neto FF. Correlation of spirometry with the six-minute walk test in eutrophic and obese individuals. Revista da Associação Médica Brasileira. 2011;57(4):387-93.

19. Soares MR, Pereira CAdC. Six-minute walk test: reference values for healthy adults in Brazil. Jornal Brasileiro de Pneumologia. 2011;37(5):576-83.

20. Dourado VZ, Vidotto MC, Guerra RLF. Reference equations for the performance of healthy adults on field walking tests. Jornal Brasileiro de Pneumologia. 2011;37(5):607-14.

21. Santos LOd, Jamami M, Di Lorenzo VAP, Ronchi CF, Arca EA, Pessoa BV. Applicability of reference equations for the six-minute walk test in healthy elderly adults in a municipality of São Paulo. Fisioterapia e Pesquisa. 2013;20(2):172-7.

22. Kundu A, Maji A, Sarkar S, Saha K, Jash D, Maikap M. Correlation of six minute walk test with spirometric indices in chronic

obstructive pulmonary disease patients: A tertiary care hospital experience. The Journal of Association of Chest Physicians. 2015;3(1):9.

23. Meriem M, Cherif J, Toujani S, Ouahchi Y, Hmida AB, Beji M. Sit-to-stand test and 6-min walking test correlation in patients with chronic obstructive pulmonary disease. Annals of thoracic medicine. 2015;10(4):269.

24. Martin C, Chapron J, Hubert D, Kanaan R, Honoré I, Paillasseur J-L, et al. Prognostic value of six minute walk test in cystic fibrosis adults. Respiratory medicine. 2013;107(12):1881-7.

25. Pereira FM, Ribeiro MÂGdO, Ribeiro AF, Toro AADC, Hessel G, Ribeiro JD. Functional performance on the six-minute walk test in patients with cystic fibrosis. Jornal Brasileiro de Pneumologia. 2011;37(6):735-44.

26. Stollar F, Rodrigues JC, Cunha MT, Leone C, Adde FV. Six minute walk test Z score: correlations with cystic fibrosis severity markers. Journal of Cystic Fibrosis. 2012;11(3):253-6.

27. Collins CE, MacDonald-Wicks L, Rowe S, O'Loughlin EV, Henry RL. Normal growth in cystic fibrosis associated with a specialised centre. Archives of disease in childhood. 1999;81(3):241-6.

28. McPhail GL, Acton JD, Fenchel MC, Amin RS, Seid M. Improvements in lung function outcomes in children with cystic fibrosis are associated with better nutrition, fewer chronic pseudomonas aeruginosa infections, and dornase alfa use. The Journal of pediatrics. 2008;153(6):752-7.

29. Gozdzik J, Cofta S, Piorunek T, Batura-Gabryel H, Kosicki J. Relationship between nutritional status and pulmonary function in adult cystic fibrosis patients. J Physiol Pharmacol. 2008;59(suppl 6):253-60.

30. Friedrich L, Pitrez PM, Stein RT, Goldani M, Tepper R, Jones MH. Growth rate of lung function in healthy preterm infants. American journal of respiratory and critical care medicine. 2007;176(12):1269-73.

31. Narang I, Baraldi E, Silverman M, Bush A. Airway function measurements and the long- term follow- up of survivors of preterm birth with and without chronic lung disease. Pediatric pulmonology. 2006;41(6):497-508.

32. Gupta B, Kant S, Mishra R, Verma S. Nutritional status of chronic obstructive pulmonary disease patients admitted in hospital with acute exacerbation. Journal of clinical medicine research. 2010;2(2):68-74.

33. Melo LC, Silva MAMd, Calles ACdN. Obesity and lung function: a systematic review. Einstein (Sao Paulo). 2014;12(1):120-5.

34. Laguna TA, Sontag MK, Osberg I, Wagener JS, Accurso FJ, Sokol RJ. Decreased total serum coenzyme-Q10 concentrations: a longitudinal study in children with cystic fibrosis. J Pediatr. 2008 Sep;153(3):402-7.

35. Agrawal MB, Awad NT. Correlation between Six Minute Walk Test and Spirometry in Chronic Pulmonary Disease. Journal of clinical and diagnostic research: JCDR. 2015;9(8):OC01.