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Research article

CORRELATION BETWEEN TOTAL ANTIOXIDANT CAPACITY AND SPIROMETRIC PARAMETERS IN BRONCHIAL ASTHMA

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Abstract

The present study aimed at measuring plasma total antioxidant capacity (TAC) and to find its correlation with lung function variables in patients suffering from bronchial asthma. Ninety two (n-92) spirometry proven asthmatics, forty nine females (n-49) with mean age 33.98 ± 11.52 standard deviation (SD) and forty three males (n-43) with mean age 35.91 ± 12.88 SD age ranging between16 to 67 were included. Thirty healthy subjects (n-30) were taken as controls with mean age 31.10 ±12.22 standard deviation (SD). The patients showed TAC value ranging between 6.4 to 24.8 with mean value 11.46 ± 4.34 SD. The controls showed TAC value ranging between 9 to 21.8 with mean value 14.62 ± 4.56 SD had significant p-value less than 0.001 ($P<0.001$).The spirometry was significant among asthmatics and controls. Several correlations were done between spirometric parameters and TAC. FEV_1, FVC, and PEF were put as independent variable and significant correlation was found between TAC with R^2=0.9583, R^2= 0.7473, and R^2= 0.1279 respectively. Our findings suggest that total antioxidant Capacity is highly correlated with spirometric parameters in bronchial asthma.

Key words: TAC, Asthma, Spirometry

Introduction

The imbalance between Reactive Oxygen Species (ROS) and anti-oxidants produce oxidative stress in asthma. It can also be implied that asthma like most other chronic illnesses may result into oxidant/anti-oxidant imbalance. [1] A low antioxidant capacity in plasma suggests an increased oxidant burden in the blood. The accurate assessment of oxidative stress in biological systems is a problem for all investigators working on the role of free radical damage in disease. The concept of a single test that might reflect total antioxidant capacity (TAC) is an attractive one as low total antioxidant capacity could be indicative of oxidative stress or increased susceptibility to oxidative damage. [2] No single component of serum antioxidant complex could fully reflect the protective efficiency of blood, probably because of interactions that occur in vivo among different antioxidant compounds. Total antioxidant capacity (TAC) considers the cumulative effect of all antioxidants present in blood and body fluids. [3] Although the concentration of plasma antioxidant components can be measured individually, these measurements may be time- and cost-consuming and labour intensive. In addition, it may not accurately reflect the total antioxidant status. [4] Thus, the accurate antioxidant capacity of the organism can only be determined by the measurement of total antioxidant capacity.[5] It possibly could be used to assess the real change in antioxidant status in patients with bronchial asthma and might lead to universally useful treatment for the chronic respiratory disorder.

The diagnosis of asthma is usually based on the characteristic symptoms. However, measurements of lung function, and particularly the demonstration of reversibility of lung function abnormalities, greatly enhance diagnostic confidence. [6] This is because patients with asthma frequently have poor recognition of their symptoms and poor perception of symptom severity, especially if their asthma is long standing. Concepts of asthma severity and control are important in the evaluation of patients and their response to treatment. The most clinically useful concept of asthma severity is based on the intensity of treatment to achieve good asthma control. [7] Assessment of symptoms such as dyspnoea and wheezing by physicians may also be inaccurate. Measurement of lung function provides an assessment of the severity of airflow limitation, its reversibility and variability, and provides confirmation of the diagnosis of asthma. Spirometry is the measurement of lung function which provides an assessment of the severity of airflow limitation, its reversibility and variability, and provides confirmation of the diagnosis of asthma. [8]

Various methods are available to assess airflow limitation, but two methods have gained widespread acceptance. These are measurement of peak expiratory flow rate and spirometry, particularly the measurement of forced expiratory volume in first second (FEV_1) and forced vital capacity (FVC) and peak expiratory flow (PEF).[9] The differentiation is made on the basis of reversibility of FEV_1 in asthma, whereas COPD shows partial or no reversibility. [10] FVC may be reduced by airflow obstruction as well as by restriction of the airways.

Normally total Lung capacity (TLC) is limited by the elasticity of the thoracic cage and the fibrous and elastic tissues of the lungs and by the strength of the muscle of inspiration. This varies with age but is affected by the course of disease. Respiratory muscle weakness reduces inspiratory and expiratory capacity and this decreases vital capacity (VC). Measurement of VC (figure- 4) is therefore an excellent means of detecting respiratory muscle weakness. [11] Reduction of TLC is termed ‘Restriction’. Restrictive ventilatory disorders include pulmonary fibrosis (e.g. interstitial pneumonia), thoracic deformity (e.g. scoliosis) or limitation (e.g. ankylosing spondylitis), lung or lobar resection, and weakness of some or all of the inspiratory muscles. In air flow

obstruction, residual volume (RV) is increased and TLC is normal or high depending on the elasticity of the lungs. Obstruction and restriction may co-exist. Obstruction increases RV and restriction increases TLC. The representation of maximal flow is particularly useful in demonstration of the following:

Reduction of maximal expiratory flow during the middle of forced expiration is caused by small airways disease and can be an early sign of airway damage, which may be present even when FEV_1 and FVC are normal. Flow limitation during tidal breathing impedes the normal increase in the rate and depth of tidal breathing during exertion. When tracheo-bronchial collapse occurs in emphysema, peak flow is relatively well preserved but flow rates diminish early in expiration. In obstruction of the airways outside the thorax, flow tends to be constant throughout the first part of expiration, rather than decelerating. [12]

The main objective of this study is to analyze, match with healthy controls and correlate the total antioxidant capacity with spirometric parameters in asthmatic patients. Whether duration of illness has any correlation with TAC has to be found. We measured plasma antioxidant capacity and correlated these with lung function in healthy controls and in patients with asthma. The total antioxidant capacity may be an augmental diagnostic and treatment tool for spirometric parameters.

Materials and Methods

Ninety two spirometry proven cases of asthma between the ages of 16-67 years, of either gender, selected at random were included in the study. All other causes of dyspnoea were excluded on the basis of clinical evaluation as well as appropriate investigation. 30 healthy adults of both sexes without any significant past medical/surgical history were subjected to spirometry and enrolled as healthy controls.

Their blood samples were drawn for TAC analysis from the plasma. Disposable syringes from Becton and Dikinson (BD) were used. All chemicals were of analytical grade except where otherwise stated. Distilled water, double distilled water and de- ionized water were used for preparing solutions wherever required.

The patients were also subjected to spirometry. Portable handheld electronic Spirometer Micromedical plus model 1999, Micromedical Ltd. Kent, U.K. was used to do spirometry. A calibration of the spirometer was performed with a 3 liters syringe prior to commencement of the study according to the recommendations of the National Asthma Education Programme. [13] A daily calibration of the spirometer was not required with the model used in this study. Spirometry variables were measured for a series of at least 3 acceptable forced expiratory readings. [14] The guidelines by American Thoracic Society (ATS) were followed for obtaining satisfactory spirometric values. [15] The best values were selected.

Results

Forty nine females (n-49) out of ninety two patients (n-92) were between the ages of 16 to 67 years with mean age 33.98 ± 11.52 standard deviation (SD). Forty three (43) out of ninety two patients were males (n-43) age ranging between 16 to 67 with mean age 35.91 ± 12.88 SD were included in the study. Thirty subjects (n-30) were taken as controls, out of which eight (9) were females with mean age 31.25 ± 10.77 SD and twenty one (21) subjects were males with mean age 31.05 ± 12.95 SD. (Table-1)

Table-1: Patients and Control age distribution with duration of illness

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Gender	Patients N	Mean Duration of Illness (years) ± Standard Deviation	Mean age (years) ± Standard Deviation	Control N	Mean age (years) ± Standard Deviation
Female	49	8.63±9.95	33.98±11.52	9	31.25±10.77
Male	43	16.25±14.63	35.91±12.88	21	31.05±12.95
Total	92	12.19±12.87	34.88±12.14	30	31.10±12.22

Spirometry

All the patients were subjected to spirometry. The comparison of spirometric values Forced expiratory volume in first second (FEV_1), Forced vital capacity (FVC), Peak Expiratory Flow (PEF) and Percentage Ratio (FEV_1/FVC) between patients and controls were applied to all the cases. FEV_1 was 1.91±0.83SD in patients and 2.93±0.80SD in controls with highly significant p-value less than 0.001(P<0.001) showing 34.8% change. FVC was 2.20±0.90 SD in patients and 3.15±0.93 SD in controls with highly significant P value less than 0.001(P<0.001) showing 30.2% change. PEF was 247.80±122.70 SD in patients and 428.20±150.02 SD in controls with highly significant P value less than 0.001 (P<0.001) showing 42.12% change. However, FEV_1/FVC was 86.21±16.60 SD in patients and 93.50±7.15 SD in controls with P value more than 0.05 (p>0.05) was not found significant as expected showing only 7.8 % change. (Table-2, Figure1-4)

Table-2: Comparison of FEV_1, FVC, PEF, FEV_1/FVC and TAC between Patients and Controls

Variables	Range Patients	Patients n-92 Mean ± SD	Range Control	Controls n-30 Mean ± SD	Significance
FEV_1 (l)	0.47-3.91	1.91±0.83	1.60-4.39	2.93±0.80	<0.001
FVC (l)	0.42-5.33	2.20±0.90	1.63-5.32	3.15±0.93	<0.001
FEV1/ FVC (%)	44-100	86.21±16.60	77-100	93.50±7.15	>0.05
PEF (l)	54-595	247.80±122.70	148-798	428.20±150.02	<0.001
TAC (m mol/dl)	6.4-24.8	11.46 ± 4.34	9.0-21.8	14.62 ± 4.56	<0.001

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Total Antioxidant Capacity

All the subjects were analyzed for TAC. The patients (n-92) showed TAC value ranging between 6.4 to 24.8 with mean value 11.46 ± 4.34 SD whereas the controls (n-30) showed TAC value ranging between 9.0 to 21.8 with mean value 14.62 ± 4.56 SD. This was highly significant with p-value less than 0.001 ($P<0.001$) showing 21.16% change. (Table-2, Figure 5)

Linear Regression

Several correlations were done between spirometric parameters and TAC. FEV_1, FVC, and PEF were put as independent variable and significant correlation was found between TAC with R^2=0.9583, R^2= 0.7473, and R^2= 0.1279 respectively. (Figures 6, 7 and 9) FEV_1/FVC and TAC with R^2= 0.3588 were insignificant. (Figure 8)

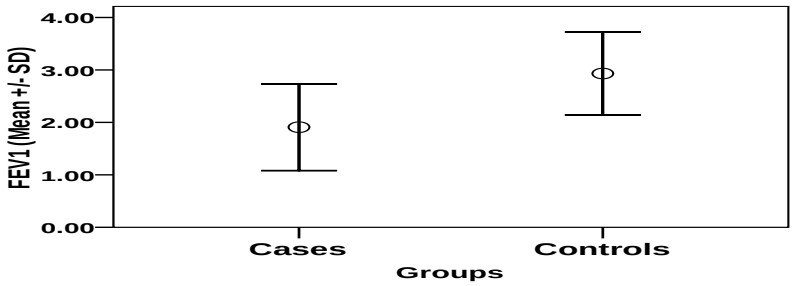

Figure 1: Comparison of spirometric values Forced expiratory volume in first second (FEV_1) between patients and controls

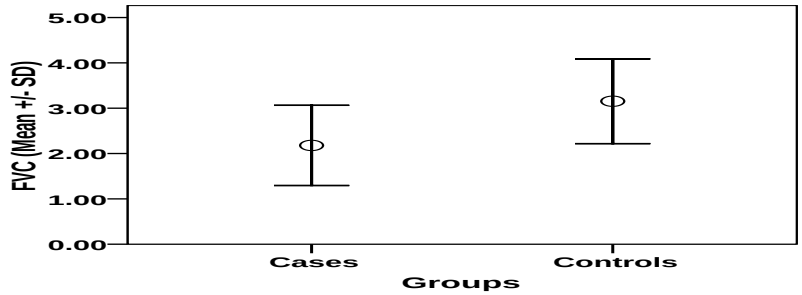

Figure 2: Comparison of Forced vital capacity (FVC) between patients and controls

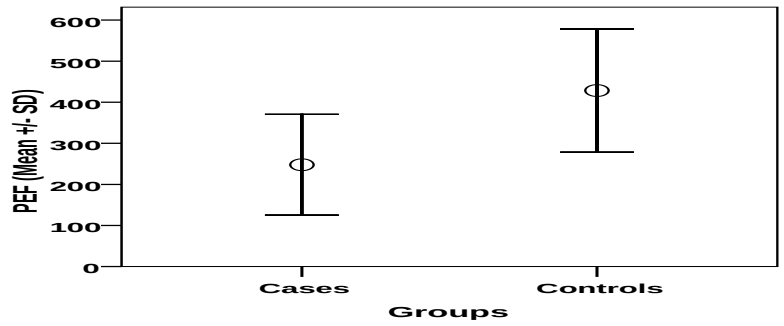

Figure 3: Comparison of Peak Expiratory Flow (PEF) between patients and controls

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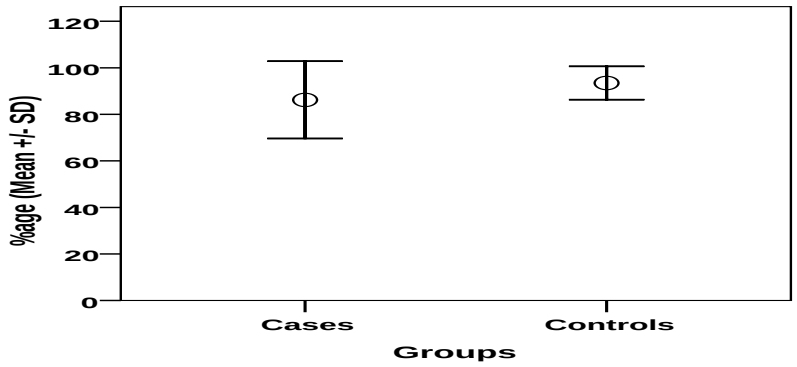

Figure 4: Comparison of Percentage Ratio (FEV_1/FVC) between patients and controls

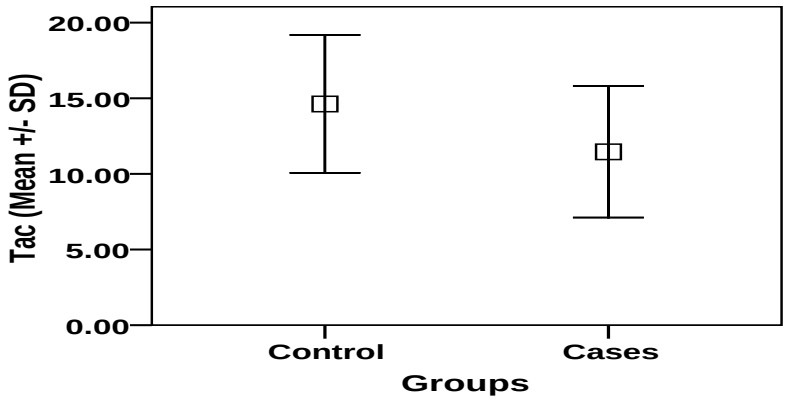

Figure 5: Comparison of Total Anti-Oxidant Capacity (TAC) between patients and control

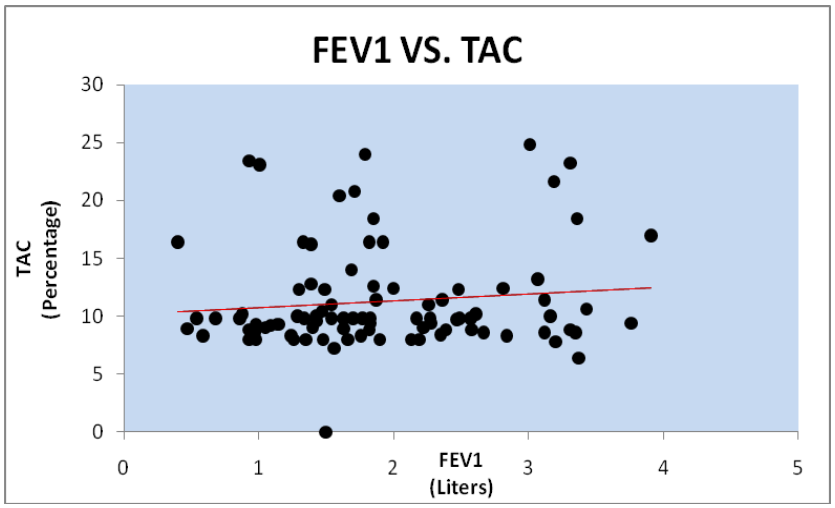

Figure 6: Correlation between FEV_1 and TAC in Asthmatics R^2=0.9583

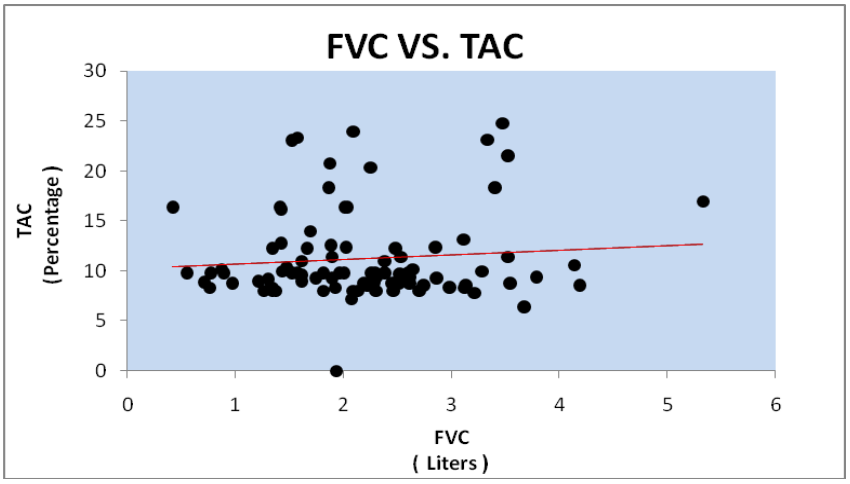

Figure 7: Correlation between FVC and TAC in Asthmatics R^2= 0.7473

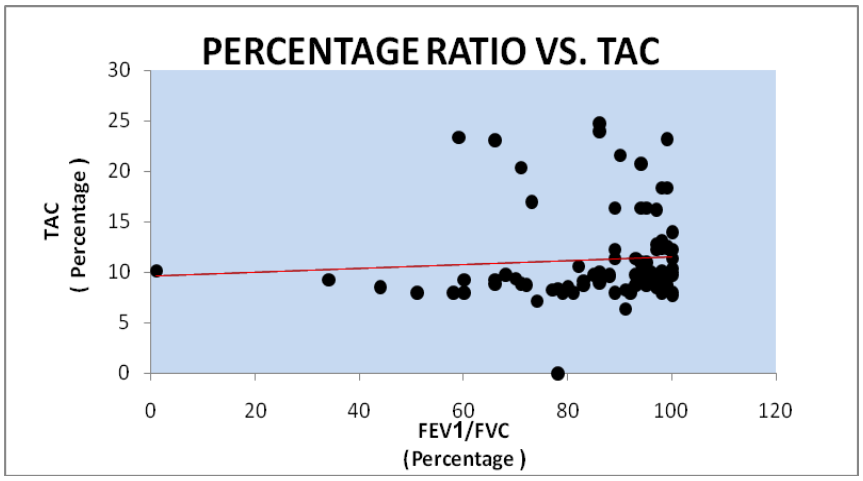

Figure 8: Correlation between FEV_1/FVC and TAC in Asthmatics R^2= 0.3588

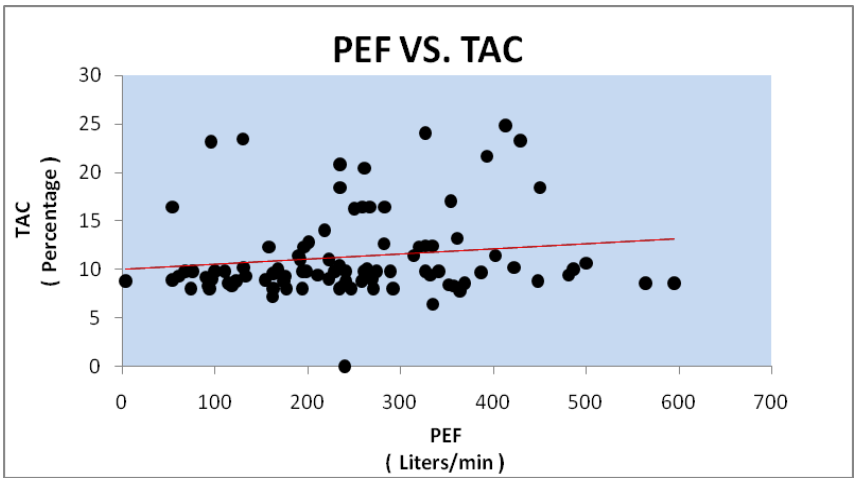

Figure 9: Correlation between PEF and TAC in Asthmatics R^2= 0.1279

Discussion

Many cells and cellular elements are affected and play a role in the progression of disease; hence asthma like most other chronic illnesses may result into oxidant/anti-oxidant imbalance which can also be assessed with TAC. Standard guidelines were followed to obtain spirometric parameters as suggested by American thoracic society. [15] The level of significance between patients and controls was consistent with the diagnosis of asthma as suggested by GINA [6] in this study. Asthmatics and normal healthy subjects were also analyzed for TAC. There was remarkable statistical difference in TAC between asthmatics and controls.TAC showed significant relationship among patients and controls.

The accurate assessment of oxidative stress in biological systems is a problem for all investigators working on the role of free radical damage in disease. The concept of a single test that might reflect total antioxidant capacity (TAC) is an attractive one as low total antioxidant capacity could be indicative of oxidative stress or increased susceptibility to oxidative damage. [2] No single component of serum antioxidant complex could fully reflect the protective efficiency of blood, probably because of interactions that occur in vivo among different antioxidant compounds. Total antioxidant capacity (TAC) considers the cumulative effect of all antioxidants present in blood and body fluids. [3] Although the concentration of plasma antioxidant components can be measured individually, these measurements may be time and cost-consuming and labor intensive. In addition, it may not accurately reflect the total antioxidant status. [4] Thus the accurate antioxidant capacity can only be determined by the measurement of total antioxidant capacity. [5] Katsoulis [16] assessed severity of asthma as decreased total anti oxidant status (TAS) which was found during an asthma attack. The TAS change was correlated with severity criteria, such as FEV_1. Therefore, it seems that measurement of TAS could be a simple and useful tool in the evaluation of an asthma attack. In our study TAC was decreased by 21.16% in asthmatics as compared to normal healthy controls showing overall reduced antioxidant status. Also FEV_1 showed 34.80% change in asthma patients. TAC and FEV_1 both decreased significantly indicating relevance of the antioxidant capacity in the chronic inflammatory disorder. The significant correlation between TAC and FEV_1 was found. Similarly FVC and PEF were also decreased showing 30.20% and 42.12% change respectively along with decrease in TAC. Measurement of serum total antioxidant capacity level was reported to provide an integrated index, as opposed to one based on simple summation of measurable antioxidants. [17] Similar to our results in asthma TAC also showed relevance in other chronic illnesses like HIV-1 positive patients. There was significant decrease in sympotomatic as compared to asymptomatic group. [5] Vaishali [18] used TAC in evaluation of antioxidant status in patients undergoing liver transplantation before and after reperfusion and showed that TAC decreased further after the procedure. Serum TAC was shown as a marker of oxidative stress in sepsis. The Acute Physiology and Chronic Health Evaluation (APACHE) II score was used for clinical evaluation of the severity of sepsis. Significant correlations were found between TAC and APACHE II. [19] Similiarly in asthma we found significant correlations amongst TAC, FEV_1, FVC and PEF. However, no relationship was found between protein thiols or TAC levels and measurements of airflow limitation in either smokers or in patients with COPD although decreased antioxidant capacity in smokers and patients with COPD indicated the presence of systemic oxidative stress. [20] It showed that there was oxidative stress in smokers and COPD but no correlations with lung function variables were found in contrast to our study in which strong correlations were found between TAC and spirometry.

In another study in Japan serum TAC and extra cellular proteins (ECP) levels were measured, and symptom scoring, spirometry, and bronchial provocation with methacholine were performed. Then, the patients were randomised to use either placebo or oral zafirlukast (40 mg/day) in addition to budesonide for 6 weeks. At the 6th week, symptom scoring, spirometry, and bronchial provocation tests were repeated and serum TAC and ECP levels were measured again. After add-on zafirlukast treatment to budesonide, forced expiratory volume in first second (FEV_1), TAC and ECP values did not change significantly ($p > 0.05$) but bronchial hyperresponsiveness and symptom score decreased significantly compared to baseline showing that such treatment may provide symptomatic relief without altering the course of decease. [21] The TAC can also be used as a marker of therapeutic outcome resulting in decreased oxidative stress. Therefore it was concluded that TAC is another reliable parameter which can be used in the cumulative assessment of antioxidant status in bronchial asthma. The measurement of individual antioxidant concentrations can be cost and time consuming whereas TAC as a single test reflects overall antioxidant capacity of the organism not only in bronchial asthma but also in other chronic inflammatory conditions. This test considers the cumulative effect of all antioxidants present in the blood and body fluids.TAC can be reliably used in evaluation of the severity of bronchial asthma along with spirometry. In yet another study on smokers the oxidative stress was assessed and shown to reduce after giving nutraceutical formulations using TAC as one of the assessment tool. [22] In acute severe asthma it is technically difficult to perform spirometry; however, TAC can be measured from the blood under such situations although it is not a replacement for spirometry which still remains the gold standard for diagnosis and assessment of asthma. Also, it can be used to ascertain the progress of the patient on follow up to assess the success of disease modification. Thus antioxidant status can be assessed along with spirometry in diagnosis and evaluation of asthma to help better management.

Conclusion

Total antioxidant capacity is highly correlated with spirometric parameters in bronchial asthma demonstrating a direct relationship.

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