Original Article

Correlation Of Serum YKL-40 With Anthropometric Measurements And Spirometric Indices Between Healthy Individuals And Asthamatics In A Tertiary Care Hospital

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ABSTRACT:

Objective: To correlate serum levels of YKL-40 with anthropometric measurements and spirometric indices between normal individuals and asthmatics.

Methodology: The case control study was conducted in Department of Chest Medicine, JPMC, Karachi from the month of August 2015 till March 2016. The study recruited sixty participants after satisfying the inclusion and exclusion criteria; among those 30 were normal healthy individuals (PEF > 80% and pulse rate of 60 – 80 beats per minutes); while equal were cases of mild to moderate asthma (PEF more than 50% and pulse rate of 100 – 120 beats per minutes) matched for age and gender. Vitallograph compacta and peak flow meter was used for spirometric indices. Moreover, anthropometric measurements were age, gender, weight (kg), height (m) and body mass index (kg/m^2). Ykl-40 Elisa kit was used for serum YKL 40 levels. The data was entered and analysed using SPSS version 21 (IBM, Chicago, IL).

Result: In comparison of Spirometric Evaluation (FEV1, FVC, FEV1/FVC% and PEFR) between control and patients with mild to moderate asthma. significant difference was found in the mean values of FEV1, FVC, FEV1/FVC and PEFR between cases and controls. Significant inverse correlation was found between YKL-40 with FEV1, FVC, FEVI/FVC% and PEFR among Controls. YKL-40 was found to be significantly correlated with only FEV_1/ FVC (%) among cases with correlation co-efficient as – 0.510 (p-value < 0.004).

Conclusion: There is an inverse correlation between serum YKL-40 levels and spirometric evaluation thus as the inflammation in asthma increases, YKL-40 level upsurges and causes decrease in lung function tests.

Key Word: Asthma, YKL-40, anthropometric, spirometric, FEV1, FVC, PEFR.

INTRODUCTION:

Asthma is a chronic lung disease of airways characterized as bronchial hyper responsiveness and inflammation as main phenomena[1-2]. Asthma is a result of multi factorial interaction in which both genetic and environmental factors plays a major and significant role[3-5]. Factors responsible for triggering or worsening the asthma symptoms including allergens (i.e. mite, dust, pollens etc.), tobacco, exercise and stress[6-7]. The asthmatics mainly complain about cough, wheezing, chest tightness, and difficulty in breathing[7].

The disease carries high morbidity and has been reported to have a high prevalence around the globe having affected people of all ages[8-9]. Approximately 300 million people are currently suffering from asthma, and it is anticipated that this count will rise up to 400 million by year 2025[10]. It has been estimated that the sufferers of asthma in Pakistan are over six million people and its prevalence is estimated to be 5% of the total population[11]. Moreover, in Karachi the biggest metropolitan city of Pakistan, about 8-10% of population which are suffering from long term asthma and approximately every 250th death is the result of severe asthma exacerbations[12].

Considering the prevalence of asthma, number of hospitalizations, emergency room visits and mortality rate as a result of severe asthma have increased in recent years, researches have been carried out to better understand the pathogenesis, the early diagnosis and clinical efficacy of treatment modalities have been carried out. Since last two decades, global and national initiatives directing on the treatment and prevention of asthma have been established carrying out the same goals described earlier[13-14]. Spirometry is the lung function test of great importance to diagnose asthma and to monitor the effects of treatment. FEV1 (forced expiratory volume in first second) and FVC (forced vital capacity) are the most important measurements can be done from spirometry along with, monitoring the PEFR that is useful in detecting changes in a patient's asthma control on disease severity[15-16].

YKL-40 is an N-terminal amino acids, and 40 shows its molecular mass, which is in kilodaltons (KDa)[17]. It is a heparin, collagen, and chitin binding plasma glycoprotein which belongs to the chitinase protein family. Serum YKL-40 is a quantifiable serum kitinase - like protein, which down/up regulates the innate immune reactions in inflammatory and tissue remodeling conditions, Normal range is below 40ng/ml in serum[18]. YKL-40 is now thought

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to be a novel biomarker of severe disease activity in patients having diseases related to the extent of inflammation, pathological tissue remodeling, and ongoing fibrosis[18]. In the present study it was investigated that whether the serum YKL-40 is associated with anthropometric measurements and spirometric indices between healthy and asthmatic individuals.

PATIENTS AND METHODS:

In the present case control study 60 individuals were recruited in the department of Chest Medicine, Jinnah Post Graduate Medical Centre (JPMC), Karachi from of August 2015 till March 2016. Among those 30 were normal healthy individuals; while equal were cases of mild to moderate asthma matched for age and gender. The normal healthy individuals had PEF > 80% and pulse rate of 60 – 80 beats per minutes while cases with mild to moderate asthma had PEF more than 50% and pulse rate of 100 – 120 beats per minutes. Cases and controls of age 18 to 60 years, of either gender were enrolled. The exclusion criteria followed were recurrent cough not due to asthma, patients of upper airway obstruction, emphysema, airway embolism chronic obstructive pulmonary disease, congestive heart failure, pulmonary embolism, post transplant patients, and having confirmed diagnosis of diabetes and hypertension. Similar exclusion criteria were followed for both cases and controls.

Spirometry was performed to assess the lung functions by vitallograph compacta. Forced expiratory volume (L) in first second, forced vital capacity (L) and ratio of forced expiratory volume to forced vital capacity was determined by vitallograph and peak expiratory flow rate (L/ min) was determined by conventional peak flow meter. Moreover, 5 cc of blood was drawn from cubital vein of all the enrolled subjects by using aseptic techniques and serum level of YKL-40 was determined through Elisa kit. Importantly, the anthropometric measurements i.e. age, gender, weight (kg), height (m) and body mass index (kg/m^2) were recorded on a pre-designed proforma.

For the present study ethical approval was granted by the ethical committee of BMSI, JPMC, Karachi, Pakistan for conducting the research. Written informed consent was obtained from all participants prior to recruitment having explained comprehensively the process involved and benefits/ risks of being the part this research. It was ensured that anonymity and confidentiality of enrolled participant's data was maintained throughout the research and no unauthorized person had an access to the data.

The data was entered and analysed using SPSS version 21 (IBM, Chicago, IL). The data was validated twice for incorrect entries. The quantitative variables were presented as mean ± standard deviation, while the qualitative variables were presented as frequency/ percentage. The anthropometric measurements i.e. age, weight (kg), height (m) and body mass index (kg/m^2) were compared between cases and controls using independent t – test. Moreover, chi square was used to compare proportion of gender between cases and controls. Furthermore, the FEV_1 (L), FVC (L), ratio of FEV_1/ FVC (%) and PEFR (L/min) and serum YKL levels were also compared between cases and controls. Importantly, separately the correlation was performed for both cases and controls between serum YKL-40 with anthropometric and spirometric evaluations. For all inferential statistics, the p-value < 0.05 was considered significant.

RESULTS:

The table 1 gives details of the comparison of anthropometric measurements between controls and cases. Among anthropometric measurements (age, weight, height and body mass index) significant difference was only found in height between the two groups. Cases with mild to moderate asthma had significantly higher mean height as compared to controls (1.63 Vs. 1.67; p-value = 0.025). Moreover, significant difference in proportion of family history of asthma was also found between controls and cases (20% vs. 56.7%; p-value = 0.007). Significant difference was found in the mean values of FEV1 (2.19 ± 0.5 Vs. 1.76 ± 0.79; p-value = 0.013), FVC (2.51 ± 0.57 Vs. 2.15 ± 0.62; p-value = 0.022), FEV1/FVC (88.41 ± 7.17 Vs. 69.92 ± 9.99; p-value = 0.001) and PEFR (327.83 ± 80.52 Vs. 198.00 ± 60.14; p-value = 0.001) between control and cases.

The table 2 gives details of the correlation of YKL-40 and spirometric evaluations (FEV1, FVC, FEV1/FVC% and PEFR) among controls. None of the anthropometric measurements (age, weight, height and body mass index) were significantly correlated with YKL-40. However, among controls YKL-40 was found to be significantly correlated with the following spirometric parameters FEV_1 (L), FEV_1/ FVC (%) and PEFR (L/min). The correlation between YKL-40 and FEV1 was negative with correlation co-efficient as – 0.565 (p-value < 0.001). The correlation between YKL-40 and FEV1/FVC% was negative with correlation co-efficient as – 0.408 (p-value = 0.025). The correlation between YKL-40 and PEFR was negative with correlation co-efficient as – 0.633 (p-value < 0.001)

The table 3 gives details of the correlation of YKL-40 and spirometric evaluations (FEV1, FVC, FEV1/FVC% and PEFR) among cases (patients with mild to moderate asthma). The YKL-40 was not found significantly correlated with any of the anthropometric measurements (age, weight, and body mass index) except height. The correlation between YKL-40 and height (m) was positive with correlation co-efficient as 0.404 (p-value < 0.027). However, among spirometric parameters YKL-40 was found to be significantly correlated with only FEV_1/ FVC (%). The correlation between YKL-40 and FEV_1/ FVC (%) was negative with correlation co-efficient as – 0.510 (p-value < 0.004).

DISCUSSION:

The present study conducted that aimed to identify whether

Anthropometric and Spirometric parameters	Controls (n = 30) n (%) OR Mean ± SD	Cases (n = 30) n (%) OR Mean ± SD	P-value
Age (years)	36.87 ± 7.87	39.10 ± 13.09	0.427
Gender			
- Male	12 (40)	11 (36.7)	0.791
- Female	18 (60)	19 (63.3)	
Weight (Kg)	65.13 ± 10.40	70.33 ± 14.04	0.108
Height (meters)	1.63 ± 0.05	1.67 ± 0.09	0.025*
Body Mass Index (Kg/m^2)	24.51 ± 3.79	24.90 ± 3.53	0.687
Family History of Asthma			
- Yes	6 (20)	17 (56.7)	0.007**
- No	24 (80)	13 (43.3)	
FEV_1 (L)	2.19 ± 0.50	1.76 ± 0.79	0.013*
FVC (L)	2.51 ± 0.57	2.14 ± 0.62	0.022*
FEV_1/ FVC (%)	88.40 ± 7.17	69.92 ± 9.99	0.001**
PEFR (L/min)	327.83 ± 80.52	198.00 ± 60.14	0.001**

Table 1. Comparison of anthropometric measurements and spirometric evaluations between controls and cases (Mild to moderate asthmatic patients)

Anthropometric and Spirometric parameters	Correlation co-efficient	P-value
Age (years)	0.115	0.546
Weight (Kg)	-0.231	0.219
Height (meters)	-0.288	0.122
Body Mass Index (Kg/m^2)	-0.137	0.472
FEV_1 (L)	-0.565	0.001**
FVC (L)	-0.322	0.082
FEV_1/ FVC (%)	-0.408	0.025*
PEFR (L/min)	-0.663	0.001**

Table 2. Correlation of YKL-40 with anthropometric measurements and spirometric evaluation among controls

Anthropometric and Spirometric parameters	Correlation co-efficient	P-value
Age (years)	0.164	0.386
Weight (Kg)	0.329	0.076
Height (meters)	0.404	0.027*
Body Mass Index (Kg/m^2)	0.138	0.468
FEV_1 (L)	-0.287	0.124
FVC (L)	-0.238	0.205
FEV_1/ FVC (%)	-0.510	0.004**
PEFR (L/min)	-0.344	0.063

Table 3. Correlation of YKL-40 with anthropometric measurements and spirometric evaluation among cases (Mild to moderate asthmatic patients)

the serum YKL-40 is associated with anthropometric measurements and spirometric indices between healthy controls and asthmatic individuals considered as cases. The results of the present study highlighted that cases with mild to moderate asthma had significantly higher mean level as compared to controls. There was significant difference between mean values of spirometric evaluations FEV_1 (L), FVC (L), ratio of FEV_1/ FVC (%) and PEFR (L/min) between controls and cases. Moreover, among controls YKL-40 was found to be significantly correlated with the following spirometric parameters FEV_1 (L), FEV_1/ FVC (%) and PEFR (L/min). Importantly, positive correlation was identified between YKL-40 and height (m) and YKL-40 was negatively correlated with FEV_1/ FVC (%) with correlation co-efficient as – 0.510 among cases.

Asthma is a disease, which is not only significant in terms of morbidity, mortality and quality of life of the patient being affected but also places an economic burden on scarce health resources[19-20]. This disease has multidimensional aspects and asthma exacerbation impact both patients and their families[21].

The present study also reported the significant difference in the mean FEV1, FVC, FEV1/FVC and PEFR between control and cases. Similar results were reported by Saba et al. (2014) showing significant difference in FEV1, FEV1/FVC between control and asthmatics[22]. Another study reported a decrease in the FEV1/FVC ratio as asthma severity increases[23]. A study also reported that severe asthma

exacerbation may result in an accelerated loss of pulmonary function as patients who frequently experienced asthma exacerbation showed a greater annual decline in FEV1 than those with infrequent exacerbations[24].

In the present study conducted we observed significant negative correlation between YKL-40 with FEV1, FEV1/FVC and PEFR in asthmatics[25]. The study conducted by Duru et al. (2013) also showed significant negative correlation between YKL-40 and FEV1, FEV1/FVC.[25] Another study reported a significant negative correlation between YKL-40 and PEFR among asthmatic patients[26].

The study has certain limitations. Firstly, the patients with severe asthma were not enrolled as it was not possible to perform spirometric evaluations due to critical health conditions. Secondly, it was difficult to find patients having asthma (cases) without any additional diseases. Thirdly, the present case control study had limited sample size with thirty cases and controls. Increasing the sample size would increase the generalisibility of the research findings.

CONCLUSION:

The study concluded that there is an inverse correlation between serum YKL-40 levels and spirometric evaluation; FEV_1 (L), FEV_1/ FVC (%) and PEFR (L/min) showing that, as the inflammation in asthma increases, YKL-40 level upsurges and causes decrease in lung function tests.

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