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Comparison of serum YKL- 40 levels between healthy adults and asthmatics in a tertiary care hospital

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Abstract

Objective:The study aim was to compare serum YKL-40 levels among controls and asthmatic patients with different severity.

Material and Methods: The case control study was conducted inDepartment of Chest Medicine, JPMC, Karachi from the month of August 2015 till July 2016. The study recruited ninety 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 30 were cases of mild to moderate asthma (PEF more than 50% and pulse rate of 100 – 120 beats per minutes) and remaining thirty were cases of severe asthma (PEFR more than 50% and pulse rate greater than 120 bpm) matched for age and gender. Vitallograph compacta and peak flow meter was used for spirometric indices. Moreover, anthropometric measurements i.e. age, gender, weight, height, body mass index and family history of asthma was recorded. Ykl-40 Elisa kit was used for serum YKL-40 levels. Statistical software SPSS version 21 (IBM, Chicago, IL) was used to enter and analyse data.

Results: There was no significant difference found in anthropometric measurements among the three groups compared. However, the patients with severe asthma had higher proportion of family history of asthma (66.7%), followed by mild to moderate asthma (56.7%) and least among the control group (20%). The significant difference was found in all spirometric parameters i.e. FEV1, FVC, ratio of FEV1/ FVC and PEFR between the control (Group I) and Cases (Group II). Significant difference in serum YKL-40 level (p-value < 0.001) was observed among the three groups. The patients with severe asthma had highest mean serum YKL-40 level (219.45 ng/ ml); followed by patients with mild to moderate asthma (95.25 ng/ ml); and least in the control group (16.14 ng/ ml).

Conclusion: The serum YKL-40 level was found elevated in patients with severe asthma compared to mild to moderate asthmatics and controls. Importantly, serum YKL-40 level had been identified as a better biomarker in patients requiring follow-up for asthma severity.

Keywords: Asthma, YKL-40, anthropometric, spirometric, FEV1, FVC, PEFR

Introduction:

Asthma is a chronic lung disease of airways being characterized as bronchial hyper responsiveness and inflammation.[1] The chronic illness is a consequence of multi-factorial interaction where both genetic and environmental factors play a major and significant role.[2] The asthmatics mainly complain about cough, wheezing, chest tightness, and difficulty in breathing.[3] Evidence from the literature has reported factors responsible for triggering or worsening the asthma symptoms including allergens (i.e. mite, dust, pollens etc.), tobacco, exercise and stress.[3,4] The disease had high prevalence and affect people of all ages with around 300 million people are currently suffering from asthma, and it is being anticipated to rise up to 400 million by year 2025.[5] In Pakistan, around six million people are the

victim of asthma and its prevalence is estimated to be 5% of the total population.[6] The disease being multi-dimensional 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 as well as impact both patients and families.[6,7]

Considering the increased prevalence of asthma, rise in hospitalizations/ emergency room visits, and higher mortality rate being reported 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 conducted. Global and National initiatives (GNI) directing on the treatment and prevention of asthma have been established around two decades back, carrying out the same goals as described earlier.8 Spirometry is the lung functiontest that measured FEV1 (Forced expiratory volume in first second), FVC (Forced vitalcapacity) and PEFR (Peak expiratory flow rate) are of great importance to diagnose asthma, detect changes in disease severity and to monitor the effects of treatment.[9]

Chitinases are enzymes that hydrolyze glycosidic bond in chitin, which dismantles the biological polymer structure. Mammalian chitinases has been identified as a biomarker for various inflammatory conditions.[10] YKL-40 is another important and prominent chitinase like protein, and it's higher levels are found to be associated with diseases like asthma, arthritis, liver fibrosis and cancers.[11] Recent studies linked serum YKL-40 levels with asthmatic patients.The present study aimed to identify YKL-40 can be established as an early biomarker of inflammation for asthmatic patients.

Material and Methods:
From August 2015 till July 2016 ninety participants were recruited from the Department of Chest Medicine, Jinnah Post Graduate Medical Centre (JPMC), Karachi. In this case control study, 30 were normal healthy individuals; while equal number of participants had mild/ moderate asthma and severe asthma matched for age and gender. The participants were allocated into the three groups by non-probability consecutive sampling technique. The study groups were as follows

Group I: Control group consisted of normal healthy individuals having Peak Expiratory Flow Rate (PEFR) > 80% and pulse rate of 60 – 80 beats per minute (bpm).

Group II: Mild to moderate asthmatic patients having PEFR more than 50% and pulse rate of 100 – 120 bpm.

Group III: Severe asthmatic patients having PEFR more than 50% and pulse rate greater than 120 bpm.

The control group (group I) and cases (group II and III) recruited were of age 18 – 60 years of either gender. The exclusion criteria followed were obstruction involving large airways i.e. vocal cord dysfunction, obstruction involving small airways i.e. viral bronchiolotis/ cystic fibrosis, recurrent cough not due to asthma, emphysema, post transplant patients, congestive heart failure, chronic obstructive pulmonary disease, and 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 compact and conventional peak flow meter. FEV1, FVC and ratio FEV1/ FVC was determined by Vitallograph compact Model 6600. The PEFR measured in L/ min was determined by the conventional peak flow meter.

Importantly, 5cc of blood was drawn from cubital vein of all the enrolled subjects by using aseptic techniques and serum level of YKL-40 (ng/ml) was determined. Serum YKL-40 was assayed by Enzyme Linked Immuno-Sorbent Assay (ELISA) Kit method. Kit used was Human Chitinase-3- like Protein 1 (YKL-40/ CH13L1) ELISA KIT 96T (20161207) YH BIOSEARCH. Moreover, the anthropometric measurements i.e. age, gender, weight, height, body mass index and family history of asthma

Table-1: Comparison of anthropometric measurements, family historyof asthma among Controls and Cases

Anthropometric measurements and family history of Asthma	Controls (Group I) (n = 30	Cases (Group II) (n = 30)	Cases (Group III) (n = 30)	Total (n = 90)	p-value
Age (years)	36.87 ± 7.87	39.10 ± 13.09	39.43 ± 8.70	38.47 ± 10.10	0.569
Gender					
Male	12 (40)	11 (36.7)	14 (46.7)	37 (41.1)	0.725
Female	18 (60)	19 (63.3)	16 (53.3)	53 (58.9)	
Weight (Kg)	65.13 ± 10.40	70.33 ± 14.04	68.33 ± 14.58	67.93 ± 13.17	0.307
Height (meters)	1.63 ± 0.05	1.67 ± 0.09	1.67 ± 0.09	1.66 ± 0.08	0.061
Body Mass Index (Kg/m^2)	24.51 ± 3.79	24.90 ± 3.53	24.18 ± 3.67	24.53 ± 3.63	0.754
Family History					
Yes	6 (20)	17 (56.7)	20 (66.7)	43 (47.8)	0.001
No	24 (80)	13 (43.3)	10 (33.3)	47 (52.2)	

Data presented as n (%) or Mean ± Standard deviation

Table-2: Comparison of spirometric evaluation among Controls and Cases

Spirometric evaluation	Controls (Group I) (n = 30	Cases (Group II) (n = 30)	Total (n = 90)	p-value
FEV_1 (L)	2.19 ± 0.50	1.76 ± 0.79	1.98 ± 0.69	0.013*
FVC (L)	2.51 ± 0.57	2.14 ± 0.62	2.33 ± 0.62	0.022*
FEV_1/ FVC (%)	88.40 ± 7.17	69.92 ± 9.99	79.16 ± 12.69	0.001**
PEFR (L/min)	327.83 ± 80.52	198.00 ± 60.14	262.92 ± 96.18	0.001**

Data presented as Mean ± Standard deviation

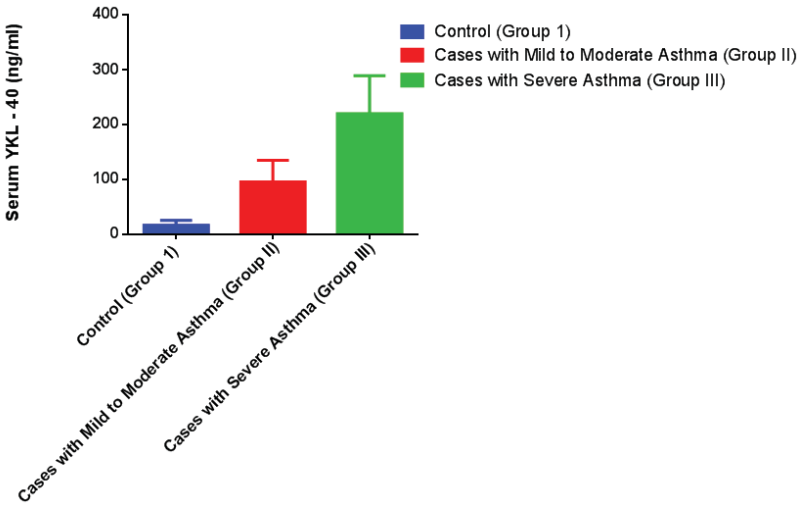

Figure. 1: Comparison of serum YKL-40 levels among Controls and Cases

were also recorded on a pre-designed proforma.

The study conducted was granted ethical approval from the ethical committee of Basic Medical Science Institute (BMSI), JPMC, Karachi, Pakistan. From all study participants prior to enrollment in the study written informed consent was obtained having comprehensively explained the process involved and benefits/ risks of being the part this research. It was also ensured that anonymity and confidentiality of enrolled participant's data was maintained throughout the research and no un-authorized person had an access to the data. The research was conducted according to the ethical guidelines of Pakistan Medical and Research Council (PMRC).

Data Analysis: The data was entered and analysed using SPSS version 21 (IBM, Chicago, IL). The data was checked 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) and importantly serum YKL-40 levels were compared among the three groups using One Way ANOVA. The post-hoc analysis (Benforoni correction) was used to identify the difference within groups. Moreover, chi square was used to compare proportion of gender and family history of asthma among the three groups. Furthermore, the mean values of FEV1 (L), FVC (L), ratio of FEV1/ FVC (%) and PEFR (L/min) were also compared between Control (Group I) and Cases (Group II) using independent t-test. For all inferential statistics, the p-value < 0.05 was considered significant.

Results:

The table 1 give details of comparison of anthropometric measurements, family history of asthma among the three group of participants; the control group (Group I), the Cases with mild to moderate asthma (Group II) and Cases with severe asthma (Group III). There was no significant difference found in anthropometric measurements (age, weight, height and body mass index) among the three groups compared. Moreover, the proportion of males and females across the three groups were also found similar with p-value > 0.725. Finally, significant difference (P-value < 0.001) was observed in family history of asthma among the three groups compared. Patients with severe asthma had higher proportion of family history of asthma (66.7%),

followed by mild to moderate asthma (56.7%) and least among the control group (20%).

Discussion:

The present study investigated asthma, a disease of immense importance and clinical significance and aimed to identify whether YKL-40 can be established as an early marker of inflammation for asthmatic patients. The results indicated that significant difference identified in the mean serum YKL-40 level among controls, mild to moderate asthmatic patients and severe asthmatic patients.

In the current study conducted we identified that greater proportion of patients with asthma had a positive family history as compared to controls, which was statistically significant. The study that recruited only children reported that greater proportion of children with asthma had positive family history.[12]

The hallmark finding of the present study was significant difference observed in serum YKL-40 level (p-value < 0.001) among the three groups. Patients with severe asthma had highest mean serum YKL-40 level (219.45 ng/ ml); followed by patients with mild to moderate asthma (95.25 ng/ ml); and least in the control group (16.14 ng/ ml). The findings were consistent with the evidence in the literature. These findings are consistent with the study by Tang et al. (2010), which compared YKL-40 level between control and asthmatics and reported that serum YKL- 40 levels were comparatively higher in asthmatics as compared to controls.[13] Moreover, the study also identified that serum YKL-40 was significantly higher in severe asthmatics as compared to mild/moderate asthmatic patients.[13] A case control study conducted in Polland reported similar findings, where mean serum YKL-40 was, with significant difference between healthy controls and asthmatics with YKL-40 were even higher in severe asthmatics compared to mild/moderate asthmatics.[14] The study by Lai et al. (2015) reported that serum YKL-40 level was higher in severe asthmatics than mild/moderate asthmatic patients.[15] As in the present study, the serum YKL-40 levels are relating with the severity of asthma, study conducted in Ankara, Turkey by Duru et al. (2013) also reported the same results and highlighted the relation of YKL-40 with severity of disease.

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. In agreement, Stout et al. (2006) found a decrease in the FEV1/FVC ratio as asthma severity increases.

The present study had certain limitations. Firstly, for patients with severe asthma it was not possible to perform spirometric evaluations due to critical health conditions. Secondly, the total IgE levels in patients with asthma, as well as in controls were not measured and related with serum YKL-40 levels. Lastly, broncho-alveolar lavage levels as well as thickness of the sub epithelial basement membrane in biopsy specimens of the lung and were further correlated with serum YKL-40 levels.

Conclusion:

The study concluded that there is a significant difference in serum YKL- 40 levels among controls and asthmatic patients. The serum YKL-40 levels were found elevated among severe asthmatic patients as compared to mild to moderate asthmatics and controls. Importantly, serum YKL-40 level has been identified as a better biomarker requiring follow-up for asthma severity. Thus, the present study recommended to use serum YKL-40 as a follow-up marker for asthmatic patients.

Conflicts of interests: No

Funding Resource: No

Role and contribution of authors:

Dr. Syed Nargis Fatima, conceived, designed, did data collection, data analysis & writing of manuscript

Dr. Shakoor Memon, review and final editing of Manuscript

Dr. Fatima Abid, literature review, data analysis and final editing of Manuscript

Dr Muhammad Abdul Samad, data analysis and final review of manuscript

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