Assessment of Fibroblast Growth Factor with Severity of Asthma

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Abstract

To evaluate the level of fibroblast growth factor 2 (FGF2) in serum of asthmatic Iraqi patients and to generate relationship between FGF2 and pulmonary function in serum of all member. FGF2 was determined in seventy Iraqi subjects; 30 diagnosed with asthma and 40 healthy subjects were registered in the revision. The age of patients and control ranged between (25-55) years. The level of FGF2 was assessed in serum by enzyme-linked immunosorbent assay (ELISA) technique. The levels of FGF2 displayed significantly increase in asthmatic group associated with control group ($p < 0.01$). Among asthmatic Iraqi patients, increase level of FGF2, indicate the significant relationship between fibroblast growth factor 2 and asthma.

Keywords: *Asthma, Fibroblast growth factor 2.*

Introduction

Asthma is one of the greatest prevalence lung sicknesses, which considered by chronic inflammation of the airways. Asthmatic patients have airway obstruction and bronchospasm as a result of greater mucous invention and changes in the buildings and purposes of some components like, fibroblasts and smooth muscle cells [(1)].

Asthma attack may occur as a result of several inflammatory events in the respiratory system lead to the appearance of sever symptom. Worldwide ,about 300 million people diagnosed with asthma and near 1000 people/ day die as a result of this disease [(2)].

Numerous elements influenced the development of asthma such as genetic tendency, environmental factors, and significant gene environment interactions [(3)].

The family of fibroblast growth factor (FGF) involves 23 members, have polypeptides and act a as powerful mitogens [(4)].

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The important member of heparin binding growth factors family is Fibroblast growth factor (FGF)-2, which affect fibroblasts growth, endothelial, and differentiation of several kind of cell. This family have important roles in morphogenesis, injury healing, infection, angiogenesis, proliferation of tumor and metastases [(5)].

Another name of FGF2 is basic FGF (bFGF) considered as the extreme member of the FGF superfamily and is the main controller of cell proliferation and variation below functional and uncontrolled disorders [(6)].

FGF-2 is universal in typical humanoid tissues and present in a link with endothelial basement membranes. FGF-2 stored in a stable formula needing become free for biological action. Proteolytic cleavage of heparin sulphate proteoglycans HSPG core proteins, the activities of glycosaminoglycan GAG destroying enzymes, and the capability of heparin to remove FGF-2 from HSPG are the mechanism for the relief of FGF-2. HSPGs are cabin professionally from extracellular via the activity of enzymes like plasmin and thrombin, and by endogenous matrix metalloproteinases (MMPs) [(7)].

Abnormality of the signaling system of FGF triggers a variety of syndromes connected with enlarged FGF level. The inhibition of FGF signaling revealed scientific effect [(8)].

Some but not all studies indicate that FGF2 is a potent fibroblast mitogen, elevated in asthmatic patients and help as an indicator for severity of asthma [9].

Methods

Ethical issues

Depending on the local ethics group the revision was agreed, all patients in this study given an idea about the purpose of the review, agree, and signed permission were informed.

Study design

This revision designated as a study of case - control.

Collection of samples

The sample size was determined according to the equation of Daniel sample size formula. The participants in the recent study include thirty Iraqi patients with asthma (depending on pulmonologist decision according to the GINA guideline), the history from them was taken, which involve: age, height, weight, gender, family history, material status and medical history, and forty apparently healthy subjects therapeutically free were serve as healthy control group. Patients with age < 6 years, non-agreement, smoker>10 pack years, patients with interstitial lung illness like unknown and drug- induced pulmonary fibrosis, chronic obstructive pulmonary disease, lung malignancy and bronchiectasis, all were excluded from the study. The age of these groups from 25 to 55 years. The statistical analysis was done with version 18 of SPSS. The findings have been expressed as Mean ± SD, and P values below 0.05 are reflected significant.

Chemicals and methods

A- Determination of human bFGF /FGF2 (Basic Fibroblast Growth Factor) by the sandwich-ELIZA kit as the method. In this kit, an antibody specific for human bFGF /FGF2 was pre-coated to the micro- ELIZA plate [10].

B- Lung function tests demonstrate the airflow obstruction that variate after little periods, either naturally or in reply to handling (reversibility) [11].

C- Simple spirometry checks airflow restriction with decreased forced expiratory volume in 1 second (FEV_1) and FEV_1 / forced vital capacity (FVC) ratio . Reversibility is established by a >12% and 200-mL elevated in FEV_1 15 minutes when an inhaled short-acting β 2 -agonist or in patients by a 2 to 4 week sample of oral corticosteroids [12]. Guidelines of national and international mention the use of spirometry for the detection and monitoring of asthma, and appear that the reversible airflow limitation is a crucial factor in the analysis of asthma. It give an idea about the amount of air you can inhale and exhale, and how fast you can empty your lungs from the air, allows clearer confirmation of airflow obstruction than the peak expiratory flow rate (PEF), and in that sense is preferable. A reduced FEV1/ VC ratio usually taken to be <70% and FEV% <80% that confirms airway obstruction [13] .

Results

The study groups consist of 70 adults designate on three categories.

1- Asthmatic patients with treatment (n=18).

2- Asthmatic patients without treatment (n=12).

3- Healthy control group (n=40).

Age

There was no significant changed in age (as mean) between control and asthmatic patients as demonstrated in table 1.

Gender

Distribution of asthma according to gender presented in Fig. 1. This study demonstrated that the incidence of asthma in female (60%) is greater than male (40%).

Body mass index (BMI)

The difference of BMI between patient and control group was non- significant (p >0.05). The mean ± SD of BMI for patients and control groups exposed in table.1.

Table (1): Demographic appearances in studied groups

	Groups	No.	Mean ± SD	P value
Age	Control	40	39.08 ± 8.96	= 0.6
	Patients	30	40.75 ± 15.30	
BMI	Control	40	31.51 ± 8.94	= 0.2
	Patients	30	29.04 ± 7.04	

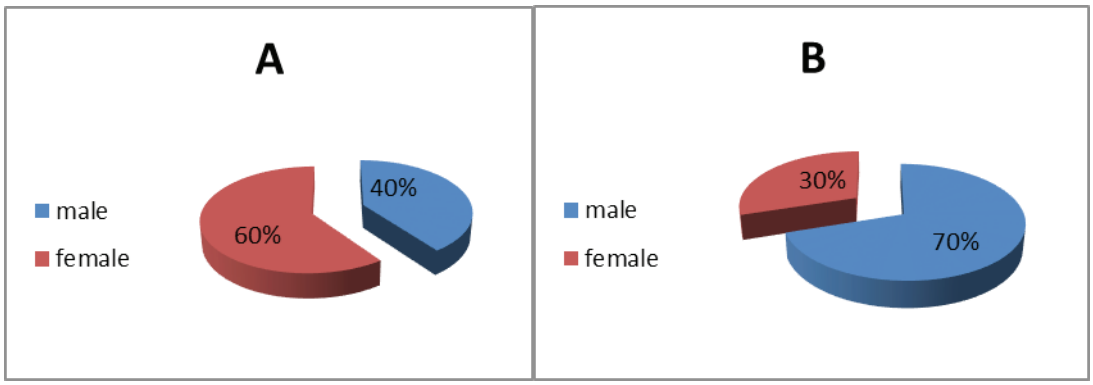

Fig (1): Gender distribution in (A) patients and (B) control

Serum level of FEV1 as mean ± SD of asthmatic patients and control.

In this study, serum concentration of FEV1 mean ± SD were significantly decrease (p<0.01) in asthmatic group when compared with control group, as shown in table 2.

Serum FGF2 concentration according to studied group.

As shown in table 2, the mean ± SD of FGF2 in asthmatic patients was (409.67± 315.12) with a significant (p < 0.001) difference likened with healthy control group.

The effect of treatment on the level of FEV1 and FGF2 in asthmatic patients.

The present study displayed significant reduction in serum level of FGF2 and significant elevated in serum level of FEV1 in asthmatic subjects with treatment than those patients without treatment, p value (< 0.001), as in table 3

Correlation of FGF2 with FEV1 in patients group

In the present study, the significant negative correlation (p value <0.01) was found for FGF2 with FEV1in asthmatic patients as in figure 2.

Table (2):Levels of FEV1 and FBF2 in studied groups

Parameters	Groups	No.	Mean ± SD	P value
FEV1	Control	40	83.7675 ± 6.60	< 0.01
	Patients	30	67.4767 ± 9.46	
FBF2	Control	40	409.6722 ± 173.95	< 0.001
	Patients	30	783.5388 ± 315.12	

Table (3): Mean differences of FGF2 and FEV1 in asthmatic patients with treatment and without treatment.

Parameters	Groups	No.	Mean ± SD	P value
FGF2	Patients with treatment	18	591.28 ± 210.49	< 0.001
	Patients without treatment	12	1071.91 ± 205.25	
FEV1	Patients with treatment	18	72.81 ± 8.55	< 0.001
	Patients without treatment	12	59.46 ± 2.45	

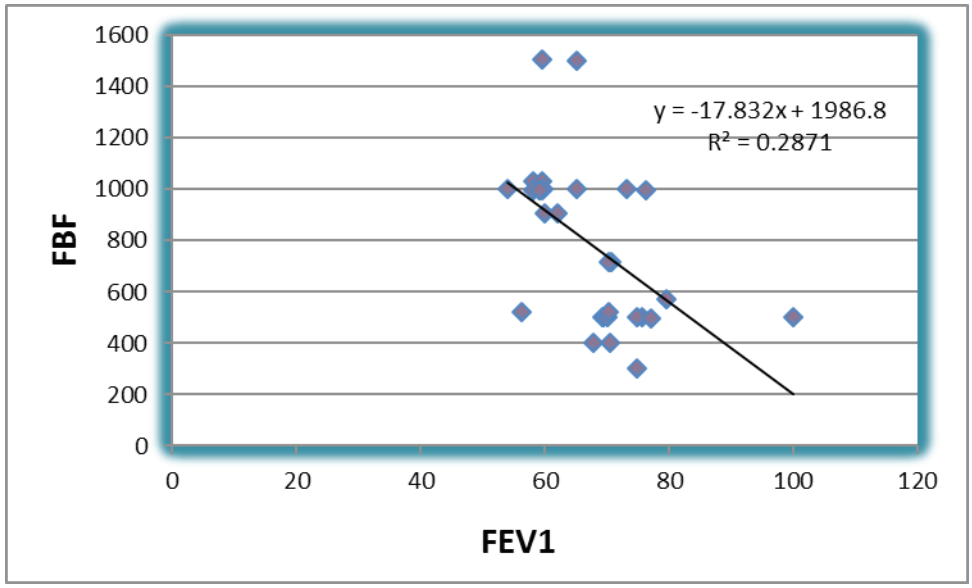

Fig (2): Correlation between FEV1 and FBG2 in patients group

Discussion

Globally, asthma revealed as the chronic lower respiratory disease. Asthma classified into mild, moderate, and severe subtypes , this classification depend on severity of asthma and rendering to fixed airflow obstruction, eosinophilic inflammation and the incidence of airway hyper-responsiveness (AHR) [(14)].

Obesity is one of the most common risk factor in asthma which helps in the improvement of metabolic disorders, chronic disease in addition to cardiovascular disease [(15)].

According to the statistics of the study, the mean age of patients who were diagnosed as asthmatic subjects and control were 40.75 and 39.08 years, respectively. The change in age (as mean) is non-significant between healthy and patients groups as shown in table 1. This age matching have a role to remove the variation in the results of different parameter that may initiate due to the variation in age [(16)]. On the other hand, this review demonstrates a slight male predominance. This finding is going with Joe G. *etal* have shown the role of sex hormones in asthma because it is sever and widespread in women, mainly in women with puberty or with multiple gestations. The main cause for gender variance are unknown but maybe linked to the immunity , hormone change, environmental and occupational exposures [(17)].

The family of FGF include different consists of polypeptides that stimulate survival, creation, and diversity of epithelial or mesenchymal cells. FGFs have a role in disease progression or regression, Dependent on the nature of the disease. There are numeral FGFs

in the lung which act as a defense system from several lethal syndromes [18].

Wound healing ,a method mentioned as airway remodeling coming after the inflammation of asthma, which produce changed in the organization of the airway including sub-epithelial fibrosis, angiogenesis, hypertrophy or hyperplasia in the airway smooth muscle [19].

Heparin and endoglycosidase produce from asthmatic lungs through that mast cells prompt the relief of FGF2 from heparan sulphate proteoglycans this make FGF2 contribute to sub-epithelial collagen deposition [20].

As showed in table 1, the FGF2 were detected in asthmatic subject than those of control group with significant variance between them ($p<0.001$). Our outcome was in agreed with [1,9] that found the same result.

Indeed, FGF2 motivate fibroblast production and the revival of epithelial cells from endogenous or exogenous stem cells, that mean FGF2 have a role in wound healing [21].

The results of this revision demonstrated that FGF2 have negative associated to the forced expiratory volume in 1 second (FEV1) in patient with asthma, our result is reliable with (Silvana Cianchetti, et al. 2019) who establish a negative relationship with the pulmonary function. The diversity in medical and inflammatory appearances of all the participant in this study responsible of conflicting results [22].

Patients with asthma response nicely to inhaled corticosteroids (ICS) treatment. Asthmatic patients have highly serum level of FGF2, and the treatment with corticosteroid diminishes it. That make FGF2 existing as a new marker for severity of asthma which linked significantly with the pulmonary function in asthmatic patients. These finding were consistent with some studies published recently [23,24].

Furthermore, higher level of FGF2 in asthmatic subject compared with control provide an idea that FGF-2 performed a defense growth factor when lung is harmed as demonstrated in table 2 and 3. These result agreed with [1,9,22,24].

Conclusion

Among asthmatic Iraqi subjects, increase levels of FGF2, indicate the significant association between asthma and fibroblast growth factor.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

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