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EVALUATION OF FETUIN A IN OBESE AND NON OBESE IRAQI WOMEN WITH FIBROMYALGIA SYNDROME

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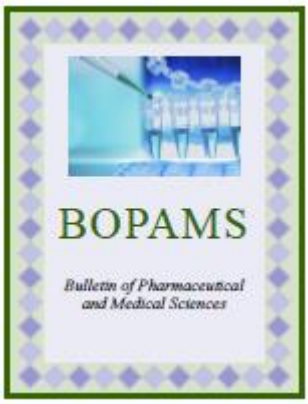

ABSTRACT

Fibromyalgia syndrome(FMS) is chronic state characterized by generalized pain associated with fatigue, stiffness, altered sleep, depression, anxiety and cognitive dysfunction. Fibromyalgia syndrome is a second common rheumatic disorder , it may to be affect 2-8% of the general population . It is the most common condition in women worldwide and causes pain all over the body . The exact cause of FMS is still unknown. Fetuin A, obesity that believed to have a key position in the pathogenesis of FMS . ***Subjects and Methods :*** eighty nine subjects between (20-55)years ; (59) patients with FMS were divided in to : (39) obese women with FMS and (20) non obese women with FMS . In addition to two controls group ;(20) obese control and (10) apparently healthy control, age and sex matched subjects as controls. Five milliliters of venous blood sample were drawn from each women ,centrifuged to obtain serum to be used for measuring the following variables : Fetuin A . ***Results*** : Fetuin A was significantly higher in FMS with obesity, while non significant in FMS with non obesity . Body mass index (BMI) is significantly higher in FMS with obesity and non significant in FMS with non obesity . A high fetuin A was associated with high BMI and tender point in FMS with obesity . ***Conclusion:*** Higher level of Fetuin A , higher BMI and tender are associated with FMS with obesity**.**

Keyword **:** Fibromyalgia syndrome , Fetuin A ,obesity, tender point

1. INTRODUCTION

Fibromyalgia syndrome (FMS) is chronic state characterized by generalized pain associated with fatigue, stiffness, altered sleep , depression , anxiety and cognitive dysfunction (1). Fibromyalgia syndrome is a second common rheumatic disorder , it may to be affect 2-8% of the general population ,it is the most common condition in women worldwide and causes pain all over the body (2). Fetuin A ,and obesity believed to have a key position in the pathogenesis of FMS . Fetuin A is Alpha 2-Heremans Schmid glycoprotein (AHSG) , with a molecular weight , 60 Kilo Dalton (kDa) and has three carbohydrate units ,which are present on a peptide chain that linked with threonine and serine residues. Fetuin A belongs to class of cysteine proteinase inhibitors. It is secreted in to serum , binds and inhibits insulin receptor tyrosine kinase in muscle and also heptaocytes ; these lead to cause insulin resistance in these target tissues (3,4) . In human ,increase fetuin A levels accompanied with obesity and insulin resistance (4,5) . Obesity has been associated with increased risk of FMS. Prevalence of obesity in patients with FMS

about 40% while in overweight , reach to about 30% (6,7) . It is not possible to assert the role that obesity plays in pathophysiology of the disease, whether it would be considered as an aggravating comorbid condition that affect FMS severity, physical dysfunction and quality of life (8,9).

Subjects, material and methods

The study was carried out over 6 months period from September 2014 till January 2015 at Medical City –Baghdad Teaching Hospital - Rheumatology and Rehabilitation Consultation Unit . This study consists of two patient groups ,the first group was composed of 39 obese women with FMS and the second group composed of 20 non obese women . In addition to two control groups ; 20 apparently healthy women as control group and 10 obese women as obese control , both matched for BMI of fibromyalgia syndrome patients . The fibromyalgia syndrome (FMS) was diagnosed by American College of Rheumatology (ACR) criteria (10). This study was approved by Clinical Research Ethics Committee of Pharmacy College University of Baghdad . Five milliliters (5ml) of Venous blood sample were drawn from each subject (patients and control).The sample placed in gel-containing tubes ,left at room temperature for at least 30 minutes for clotting, then centrifuged at 1000 round per minute (rpm) for 10 minutes in ordered to obtain serum , then separated and divided into aliquots .The serum kept frozen at -20°C until analysis used to measure fetuin A . Measurement of fetuin A level was performed by Enzyme –Linked Immune Sorbent Assay (ELISA) , using a commercially a available Kit , human fetuin A ELISA kit . The principle of this technique is based on a quantitative Sandwich –Assay by using two specific and high affinity antibodies, the plate of microliter has been pre –coated with an antibody specific to the substance to measure .The results were expressed as Nano gram per milliliter (11)

2.1. Statistical Analysis

All data analyzed using Minitab version 17 computer program . Statistical Analysis involved descriptive statistics, tables and figures . Statistical Analysis also included t-test and Person correlation coefficient test for quantitative variables. In this analysis, Person correlation coefficient was determined , p values were based on 2- sided tests and p value less than 0.05 ($p<0.05$) was considered statistically significant .

3. Result

3.1 Baseline Demographic and Clinical Characteristic

The clinical characteristic and baseline demographic of the study groups, as well as Biochemical parameters of the patients and controls as shown in table 1 and table 2 .The study group included 89 subjects 59 patients (39 FMS with obesity and 20 FMS with non obesity) and controls (20 obese control and 10 apparently healthy control) . As shown in table 1,the mean age for patients (FMS with obesity and FMS with non obesity) and controls (obese and apparently healthy controls) were 42.49±8.36 ; ;30.15±5.98 ; 36.55 ± 9.10 ; 34.2±6.01 years respectively . The mean value of age for FMS with obesity was significantly higher than obese control ,while mean value of age was non significant between FMS with non obesity than healthy control . The mean value of BMI for patients and controls were 32.55±3.99 ; 22.94±1.59 ; 29.78±3.83 ; 22.98±1.75 Kg /m^2 respectively ,the BMI of FMS patients with obesity was significantly higher than the BMI of obese control ($p < 0.05$) ,while non significant between FMS patients with non obesity and healthy control ($p > 0.05$) . Table 2 show the Mean ±SD for serum levels of in controls and patients . Fibromyalgia syndrome (FMS) with obesity showed higher level of Fetuin A than obese control ($p< 0.01$),while non significant between FMS with non obesity and healthy control($p>0.05$) .

Table 1 : Baseline Demographic and Clinical Characteristic of Women Enrolled in the Study

	Fibromyalgia syndrome (FMS) with obesity	Obese control	Fibromyalgia syndrome with non obese	Healthy control
Number of subjects	39	20	20	10
Age (year)	42.49±8.36 *	36.55 ± 9.10	30.15±5.98	34.2±6.01
BMI (kg\m^2)	32.55±3.99 *	29.78±3.83	22.94±1.59	22.98±1.75
Tender point	13.49 ± 3.66*	4.5±1.99	11.05±2.46#	1.9±0.994
Social condition **Married** **Single**	94% 5%	75% 25%	80% 20%	90% 10%
Occupation% **House wife** **Working**	89% 10%	80% 20%	85% 15%	80% 20%

Table 2 :Mean ±SD for biochemical parameters of the patients and controls

	Fibromyalgia syndrome with obesity	Obese control	P value*	Fibromyalgia syndrome with non obesity	Healthy control	P value*
Fetuin A (ng\ml)	111.8±27.6*	86.8±23.5	< 0.01	93.9±29.4	84.6±18.9	>0.05
Thyroid Stimulating Hormone(TSH)	2.03 ± 1.72	2.27 ± 1.69	>0.05	2.06 ±1.58	2.20 ± 1.67	>0.05
Total T3	1.79 ± 0.71	1.75 ± 0.48	>0.05	1.81 ±0.63	1.81 ± 0.60	>0.05
Total T4	98.3 ± 18.9	97.7 ± 17.9	>0.05	96.7 ± 18.1	100.7 ± 21.4	>0.05

P value < 0.05 considered significant

P value > 0.05 considered non significant

3.2 Correlations Studies

3.2.1 Correlation Coefficient and P values of fetuin A , BMI and tender piont among all studied groups combined.

As shown in table 3 the serum fetuinA level was positively correlated with BMI and tender piont (p <0.01)(p) respectively .

Table 3: Correlation Coefficient and P values of fetuin A,BMI and tenderpiont in FMS patients with obesity:

Variable		BMI	Fetuin A
Serum Fetuin A	**R value**	**0.337**	
	P value	**0.036***	
Tender piont	**R value**	**0.4077**	**0.333**
	P value	**0.01***	**0.038***

*(*).Correlation is significant at the 0.05 level (2 –tailed)*

4. Discussion

In this study , BMI and tender point was significantly higher in FMS with obesity than obese controls , but non significant in FMS with non obesity when compared with healthy control as shown in table 1 . This was consistent with several studies (12-14) . The definition of obesity in this study based up on the BMI . Body mass index is a vital measure for classifying obesity today , this can be due to the simplicity and measure of body composition .It is generally linked to body fat (14). Other studies also reported that FMS risk increased with BMI (15,16- 17). This can be due to reduce physical activity, stress , anxiety , poor sleep and depression , have been related with BMI in FMS obese patients .Body mass index was positively linked to fatigue , self reported pain ratings , tender piont and also tenderness threshold , so obese women with FMS is associated with higher pain severity , greater in the number of tender points ,lower sleep quality, decreased physical strength and flexibility when compared with non obese (17,18-20).

In this study , serum fetuin A levels was significantly higher in obese women with FMS than obese control while non significant in non obese women with FMS than healthy controls . In line with other studies investigating the obesity in fibromyalgia syndrome (FMS) (21- 23). Fetuin A is define as a liver secretory glycoprotein that stimulate the production of the inflammatory cytokines from adipocyte and macrophages so acts as a biomarker of chronic inflammatory disease (24) . Fetuin A knockout mice are found resistant to the weight gain on high fat diet . Hypothesis that the obesity leads to elevated fetuin A levels in obese patients is supported by the animal studies ,in a rat model of diet induced obesity , a high in fetuin A mRNA expression was found in a liver . It has been found that fetuin A acts as a major carrier protein of the Free fatty acids (FFAs) in the circulation (25) . Free fatty acids cause fetuin A over expression through NF-kB and that the elevation of Fetuin A circulatory level may increase pro-inflammatory cytokine production and suppress adiponectin production from the adipocytes (26,27) . Fetuin A may act as an endogenous ligand for TLRs so that it has a role in FFA that induced TLR4 and NF kB activation and may lead to release pro inflammatory cytokines and substances such as RNS and ROS(25) .

In present study, positive significant correlation was reported between serum fetuin A level and BMI in FMS with obesity. This study was supported by Thakkinstian *et al* . (2014) who found that serum fetuin A level were positively associated with BMI (28) .Positive significant correlation was also reported in FMS with obesity between BMI and tender point (TP) (29) .

5. Conclusion

1. Fibromyalgia syndrome with obesity is associated with higher level of inflammatory biomarker Fetuin A and tender point
2. Body mass index is significantly higher in FMS with obesity.
3. Positive association of fetuin A, BMI and tender point in FMS with obesity.

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