

LEVEL OF C-REACTIVE PROTEIN AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER

By

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ABSTRACT

Background: The relationship between inflammation and major depressive disorder (MDD) and its associated suicide has been widely debated in recent years. MDD is one of the most common psychiatric disorders, effects on about 6.7% of adult in every year and it is also one of major causes of suicide. C-reactive protein (CRP) is one of signs of inflammation in body and may have a role as an inflammatory marker in depression and associated suicide.

Objective: To find the association between depression and C-reactive protein.

Patients and Methods: The sample consisted of 25 adult diagnosed with MDD, and 15 adult were not diagnosed with any mental disorder. They were diagnosed clinically according to DSM-5 through a designed semi structured clinical interview and through application of Beck Depression Inventory-II (BDI-II) and Suicidal Probability Scale (SPS), and blood samples were taken to measure plasma level of CRP.

Results: There was a relationship between major depressive disorder and C-reactive protein where it was found that there were statistically significant differences between the cases and control groups in scores of CRP. The mean of cases were 3.88mg/L and control group was 3mg/L with P value 0.019. Moreover, there was a statistically significant difference between CRP level and degree of severity of depression on BDI-II scale. Besides that, there was a relationship in CRP of cases group when compared between depression with suicide ideations and without, yet not a statistically significant. There were also statistically significant differences between cases and controls groups on BDI-II and also on Suicidal Probability Scale (SPS).

Conclusion: C-reactive protein elevated in major depressive disorder patients, and also associated with severity of MDD although this elevation lie in normal range of CRP.

Key words: Depression; Major depressive disorder; Suicide; C-reactive protein.

INTRODUCTION

Depression (major depressive disorder) is a common and serious medical illness that negatively effects on feelings. The way of thinking and behavior, also causes feelings of sadness and/or a loss of interest in activities which previously enjoyed. It can decrease a person's functional ability and also lead to a variety

of emotional and physical problems (*American Psychiatric Association {APA}, 2013*). One in six people (16.6%) suffers from depression at some point in their lives can occur at any time of age, and affects an estimated one in 15 adults (6.7%) in any year (APA, 2013). The aggregate point, one-year and lifetime prevalence of depression calculated prevalence of 12.9%, 7.2% and 10.8%

respectively (*Lim et al., 2018*). In Egypt, total prevalence of mental disorders was 16.93%, where the main problems were mood disorders at 6.4%, anxiety disorders at 4.8% (*Okasha et al., 2012*).

Depression may be accompanied with suicide by 6.67% and 3.77% for men and women, respectively (*Nordentoft et al., 2011*). Non-fatal suicide attempts could be 40 times more common than completed suicides, and for every suicide attempt about 10 people experience suicidal thoughts (*Chang et al., 2013*). Suicide attempts are also up to 30 times more common compared to suicides, and suicide generally represents 1.4% of all deaths worldwide (*Bachmann, 2018*). Suicide in Egypt, the mean annual estimates range 0.7 to 2.2 per 100,000 populations (*Mars et al., 2014*).

Some studies reported that groups of individuals with major depressive disorder (MDD) demonstrated increased levels of a variety of peripheral inflammatory biomarkers when compared with groups of non-depressed individuals. These findings are often interpreted as meaning that MDD may be an inflammatory condition (*Raison and Miller, 2011*). Patients with major depressive disorder, who had suicidal thought or had attempted suicide, had elevated rates of inflammation compared to patients with major depressive disorders who had no suicidal tendencies (*O'Donovan et al., 2013*).

The present work aimed to find the association between depression and inflammatory process by the inflammatory biomarker C-reactive protein.

PATIENTS AND METHODS

This study was conducted at Shebin Elkom Mental Health Hospital, where 25 persons were diagnosed with major depressive disorder, and 15 persons were not diagnosed with any mental disorder during the period between November 2018 and April 2019. There was about some changes in their life and their age ranged between 18 and 60 years old. Tools were used was Beck Depression Inventory-II (BDI-II) (*Beck et al., 1996*), and Arabic version (*Ghareeb, 2000*), and Suicidal Probability Scale (*Gull and Gill., 1982*), and Arabic version (*Albehairy, 2013*) which were standardized. Blood samples were taken from two groups to measure plasma level of C-reactive protein (CRP). All patients signed informed written consents after explanation of the aim of the study and its details.

Inclusion criteria:

Age range was 18-60 years of both sexes. Case group was diagnosed as major depressive disorder, and control group have not any mental disorder.

Exclusion criteria:

Patients with any psychiatric co-morbidity or were with any acute infection or inflammation, patients who suffered from organic diseases that raise the rate of CRP such as rheumatoid arthritis, systemic lupus erythematosus, heart disease, vasculitis, hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), Alzheimer disease, Parkinson's disease, inflammatory bowel disease, and tumors.

Statistical analysis:

Data was collected and entered to the computer using SPSS (Statistical Package for Social Science) program for statistical analysis, (version 22; Inc., Chicago. IL).

Data from questionnaires was entered as numerical or categorical, as appropriate.

Two types of statistics were done:**•Descriptive statistics:**

- Quantitative data was shown as mean, SD, and range.
- Qualitative data was expressed as frequency and percent.

•Analytical statistics:

- Mann Whitney test was used to compare mean and SD of 2 sets of

quantitative when this data is not normally distributed.

- Kruskal-Wallis test was used for comparison between three or more groups when this data is not normally distributed.
- Post hoc test was used for specific differences between three or more group means when an analysis of variance.
- Spearman's correlation was used to study correlation between two variables when this data is not normally distributed.
- P value: was considered statistically significant when $P \leq 0.05$.

RESULTS

During the descriptive statistics and comparison of the sample in the term of age, gender, marital status and work, it was found that cases group sample was 25 adult while control group was 15, the mean of age of cases and control groups were 33.24 and 32.12 respectively, according to gender, in cases group was 7 males and 18 female, to marital status in

cases group was 10 single, 13 married and 2 divorced, and to work in cases group was 6 not worked, 15 worked and 4 students, to the mean of CRP in case and control groups were 3.88 and 3.00 respectively, and to CRP in case and control groups according to suicidal ideation (SI) or not **Table (1)**.

Table (1): Distributions and comparison of cases and control groups according to gender, marital status, work, age (years), C-reactive protein, and CRP according to SI

Parameters		Groups		Control group = 15		Cases group = 25		P-value
		N	%	N	%	N	%	
Gender	Male	N		7		7		0.231
		%		46.7%		28.0%		
	Female	N		8		18		
		%		53.3%		72.0%		
Marital status	Single	N		7		10		0.522
		%		46.7%		40.0%		
	Married	N		8		13		
		%		53.3%		52.0%		
	Divorced	N		0		2		
		%		0.0%		8.0%		
Work	No	N		1		6		0.331
		%		6.7%		24.0%		
	Yes	N		12		15		
		%		80.0%		60.0%		
	Student	N		2		4		
		%		13.3%		16.0%		
Age	Mean ± SD			32.13±8.967			33.24±9.888	0.725
	Median			15			25	
	(Mini-Maxi)			31.00(18-55)			33.00(18-53)	
C-reactive protein	Mean ± SD			3.00±1.414			3.88±1.269	0.019
	Median			15			25	
	(Mini-Maxi)			3.00(1-7)			4.00(1-6)	
C-reactive protein	Mean ± SD Median (Mini-Maxi)			No SI	SI	No SI	SI	0.09
		2.92±1.498	3.50±0.707	3.75±0.965	4.00±1.528			
		13	2	12	13			
		3.00	3.50	3.50	4.00			
		(1-7)	(3-4)	(3-6)	(1-6)			

According to severity of depression on BDI-II and its degrees with CRP in cases group, it was found that mean of CRP in moderate, severe and extreme severe degree were 2.6, 3.77 and 5 mg/L

respectively while there was not a minimal degree of depression, this showing that there was a statistically significant among all and between each other (**Table 2**).

Table (2): Comparison between BDI-II degrees with CRP

BDI-II CRP				P-value	Post hoc
	Moderate	Severe	Extreme severe		
Mean ± SD	2.6±1.14	3.77±0.725	5.00±1.291	0.010	(M&S) P1=0.035 (M&E) P2=0.0001 (S&E) P3=0.014
No.	(5)	(13)	(7)		
Median	3.00	4.00	6.00		
(Mini-Maxi)	(1-4)	(3-5)	(3-6)		

Note: M = moderate, S = severe, E = extreme severe

According to relationship of CRP with the other variants in cases group, there was a direct relationship between CRP

and BDI-II while there was not a relationship between others (**Table 3**).

Table (3): Correlation between CRP and the other variants

Spearman's rho CRP		CASES = 25
Suicide Probability Scale (SPS)	Correlation Coefficient	0.178
	Sig. (2-tailed)	0.395
	N	25
Suicidal ideations (SI)	Correlation Coefficient	0.151
	Sig. (2-tailed)	0.472
	N	25
Beck Depression Inventory (BDI-II)	Correlation Coefficient	0.618**
	Sig. (2-tailed)	0.001
	N	25
Age	Correlation Coefficient	0.081
	Sig. (2-tailed)	0.699
	N	25
Work	Correlation Coefficient	-0.336
	Sig. (2-tailed)	0.100
	N	25
Marital status	Correlation Coefficient	0.078
	Sig. (2-tailed)	0.712
	N	25

DISCUSSION

By comparing the sample of cases in terms of gender, it was found that 7 males and 18 females doubled the ratio. This increased rate for females corresponded to *Salk et al. (2017)* where the ratio equals twice the percentage for females compared to males, although in some studies are less as they were in the study of *Pearson et al. (2015)* where amounted to 1.6 for females compared to males.

The mean age of cases was 33.24 years, and of the control sample was 32.13. This agreed with *Liaqat et al. (2019)* where the mean age for the cases was 33.12 and for the control group was 33.72.

By comparing the sample of cases and controls in terms of marital status, it showed that the ratio in cases was 40%

single, 52% married and 8% divorced, and in the control group, 46% were single and 54% married. This was close to an Egyptian study by *Hassan et al. (2013)* for cases with major depression disorder where married cases were 75.7%, where 13.3% single, and where 10.8% divorced or widowed. This is despite the fact that depression occurs most of the time in people who do not have close personal relationships according to the study of *Spiker (2014)* as marriage is linked to a decrease in mental disorders including depression.

In comparison in terms of work for cases, the study states that 24% did not work, 60% work and 16% are students. Despite this, *Brody et al. (2018)* stated that about 80% of people with depression reported some difficulties and social

dysfunction, even if at work, at home, or at work due to symptoms of depression.

As for the level of the C-reactive protein in the cases and the control, there were statistically significant differences where the mean of the CRP in the cases was 3.88, while the control group was 3. These two rates were almost within the normal range that reaches to 5 mg/L (*Syeda et al., 2014*).

For cases where the mean CRP was 3.88. The lowest level was 1 mg/L and the highest level was 6 mg/L. This was somewhat compatible with the study (*Köhler-Forsberg et al., 2017*). This also coincide in terms of the higher rate of CRP in the cases more than the control group with this study (*O'Donovan et al., 2013*) where there was a trend towards higher levels of CRP in cases than the control group, but this was not statistically significant.

The results of the study showed that there was a direct relationship between CRP level and Beck Depression Inventory (BDI-II), where the mean CRP in moderate cases on BDI-I was 2.6 whereas in severe cases was 3.77 and it was 5 mg/L in extreme severe cases.

This corresponded to a study by *Köhler-Forsberg et al. (2017)* who showed that the greater the severity of depression, the greater the CRP level. These results were statistically significant only among females.

Regarding the level of CRP between cases and control in terms of suicidal thoughts, there was not statistically significant difference, although there was a slight increase in favor of cases where

the mean level of CRP in cases was 4 mg/L and in control was 3.5.

With the comparison of the CRP in the cases only in terms of the presence of suicidal thoughts or suicidal behavior, there was not statistically significant difference, where the mean CRP with the presence of suicidal ideations was 4 mg/L and without was 3.75.

O'Donovan et al. (2013) found that patients with low suicidal thoughts did not differ significantly from control cases in the level of CRP, but was higher in depression with higher suicidal thoughts. However, the mean of CRP in persons of control group was 1.6 mg/L versus 2.9 mg/L for cases of low suicidal thoughts, compared to 4.6 mg/L for persons of higher suicidal thought.

Liaqat et al. (2019) compared depression with or without suicide with the control sample. The CRP level was higher in suicidal depression cases than depression without suicide, and the latter was higher than the control sample and the mean was in order 6.4, 3 and 2 mg/L. Despite this increase, all ratios are located in the normal range for the level of CRP. This was consistent with the present study in increase's principle, but it was a slight increase and not statistically significant.

CONCLUSION

C-reactive protein elevated in major depressive disorder patients than healthy control, and also associated with severity of MDD, beside a slight increase of CRP in MDD with suicidal thoughts, despite of this elevation, all ratios lie in normal range of CRP.

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مستوى بروتين سي التفاعلي لدي مرضي الاكتئاب الجسيم

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خلفية البحث: قد نُوقشت العلاقة بين الالتهاب واضطراب الاكتئاب الجسيم على نطاق واسع في السنوات الأخيرة، اضطراب الاكتئاب هو واحد من أكثر الاضطرابات النفسية شيوعاً، ويؤثر على حوالي 6.7% من البالغين في كل عام وهو أيضاً أحد الأسباب الرئيسية للانتحار. بروتين سي التفاعلي هو أحد علامات الالتهاب في الجسم وقد يكون له دور كعلامة التهابية في الاكتئاب والانتحار المرتبط به.

الهدف من البحث: إيجاد علاقة بين الاكتئاب وبروتين سي التفاعلي.

المرضي وطرق البحث: بلغت العينة 25 بالغاً مصاباً باضطراب الاكتئاب الجسيم و 15 بالغاً لم يتم تشخيصهم بأي اضطراب نفسي، وتم اجراء مقابلات شبه مقننة، كما تم أخذ موافقة شفاهية وكتابية من كل المشاركين في الدراسة وذلك بعد تعريفهم بمنهج الدراسة وهدفها وحقهم في الانسحاب منها في أي وقت. وقد تم تطبيق مقياس بيك للاكتئاب، ومقياس احتمالية الانتحار، وكذلك تم أخذ عينة دم لإجراء تحليل بروتين سي التفاعلي.

نتائج البحث: كان متوسط عمر الحالات والمجموعة الضابطة 33.24 و 32.12 على التوالي، وفي الحالات حسب الجنس كان هناك 7 ذكور و 18 إناث، وبحسب الحالة الاجتماعية كان هناك 10 حالات أعزب، 13 متزوج و 2 مطلق، وبحسب العمل كان هناك 6 غير عاملين، 15 شخص يعمل و 4 طلاب.

كانت هناك علاقة بين اضطراب الاكتئاب الجسيم وبروتين سي التفاعلي حيث وُجدت فروق ذات دلالة إحصائية بين الحالات والمجموعة

الضابطة في متوسط بروتين سي التفاعلي فبلغ متوسط الحالات 3.88 مجم / لتر ومتوسط المجموعة الضابطة 3 مجم / لتر.

علاوة على ذلك كان هناك فرق ذات دلالة إحصائية بين مستوى بروتين سي التفاعلي ودرجة شدة الاكثئاب علي مقياس بيك للاكثئاب.

كان هناك أيضا فروق ذات دلالة إحصائية بين الحالات والمجموعة الضابطة علي مقياس بيك للاكثئاب و مقياس احتمالية الانتحار.

الاستنتاج: تظهر نتائج الدراسة أن بروتين سي التفاعلي مرتفع لدى مرضى الاكثئاب الجسيم, وأرتبط أيضاً بشدة الاكثئاب بالرغم من أن هذا الارتفاع يقع في المعدل الطبيعي لبروتين سي التفاعلي.