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Determination of Serum Adiponectin and Vitamin D Levels in Patients with Depression

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Abstract

Objective: In this study we aimed to determine serum levels of adiponectin and vitamin D in patients with depression. We further tried to find association between adiponectin, vitamin D and inflammatory marker, high sensitivity C reactive protein, and oxidative stress marker malondialdehyde in these patients. **Methods:** This is a cross-sectional/ analytical study carried out in the out patient's department of the psychiatry department of Hayatabad Medical Complex, Peshawar. A total of 120 participants were randomly selected and divided into two groups. Group A was labelled as Cases and consisted of 60 newly diagnosed patients with depression. Group B was labelled as Control and consisted of age and gender matched healthy participants with no major physical or mental illness. Any subject with prior anti-depressant treatment or any other major physical illness was excluded from the cases group. A fasting 5 mL blood sample was collected from all participants after well informed written consent and was analyzed for serum adiponectin, vitamin D, malondialdehyde (MDA), total anti-oxidant capacity (TAC) and high sensitivity CRP (hs-CRP). Statistical analysis was done

with SPSS version 21. Comparisons between the two groups were done with independent student's t test. Pearson's correlation co-efficient r was used to find association of adiponectin with other biomarkers. Significance of the results was considered with a p value of less than 0.05. **Results:** Adiponectin µg/mL (4.3±7.0 vs 9.4±5.5, P<0.0001) and vitamin D levels ng/mL (17.06±6.4 vs 30.81± 3.3, P<0.0001) were found to be significantly lower in cases than control. The inflammatory marker hs-CRP (mg/L) and oxidative stress marker MDA (nmol/L) were significantly higher in patients with depression (4.4±2.7 vs 1.2 ±1.1) and (5.83±0.62 vs 2.52±0.84). Adiponectin correlated significantly positively with vitamin D (r 0.45, P<0.0001), and TAC (r 0.52, P<0.0001), and negatively with hs-CRP (r-0.33, P<0.0001). **Conclusion:** Adiponectin and vitamin D were both low in patients with depression and associated inversely with inflammatory markers and oxidative stress markers i.e hs-CRP and MDA respectively. Future studies may implicate a potential combined therapeutic role of adiponectin and vitamin D supplements in these patients.

Keywords: Adiponectin, Vitamin D, Depression, hs-CRP, Malondialdehyde

Introduction

Depression is the commonest cause of disability affecting about 280 million population world-wide (1). There have been significant advances in the neuro-pharmacological modalities still around one third of the patients fail to adequately respond to the first-line anti-depressant treatment signifying the importance of a deeper understanding of its pathophysiology (2). Depression is not just a monoamine deficiency but linked to neuroendocrine dysregulation, chronic inflammation, metabolic dysfunction and oxidative stress as its core contributors (3,4).

Adiponectin and vitamin D are thought to play protective role against depression due to their anti-inflammatory and neuroactive functions respectively. Adiponectin is a 244 amino acid containing protein secreted by white adipose tissue. It not only has insulin sensitizing and anti-inflammatory function but protects the integrity of blood brain barrier and promotes hippocampal neurogenesis (5-7). Vitamin D is a steroid hormone and in addition to its proven role in calcium homeostasis, it has its receptors in brain including hippocampus, amygdala as well as prefrontal cortex (8). Vitamin D has a role in serotonin regulation (9), oxidative stress reduction (10) and suppression of inflammatory gene transcription (11).

Studies have inconsistently reported low adiponectin in depression (12,13) but have shown strong association of low vitamin D with depressive disorders (14,15). In the present study we have tried to determine adiponectin and vitamin D in a single study population. In our understanding, this is the first of its kind in our population. As both

vitamin D and adiponectin share functions like suppression of NF-κB-mediated inflammation, hippocampal neurogenesis and metabolic health (9,11,16), therefore, studying them in one study may add a synergistic effect to the already known literature on the topic.

Methodology

Study Design and Population

This was a cross-sectional and analytical study and carried out in the OPD of the psychiatry department of HMC, Peshawar. The study population was randomly selected and classified as group A cases: newly diagnosed patients with depression and group B: normal control. Any participant with major illness such as metabolic disease, diabetes, coronary heart disease, malignancy, liver, kidney disease was excluded from both groups. Any participant who has been taking any form of anti-depressants or centrally acting drugs were also excluded. A well informed written consent was obtained from the study participants. There detailed history, demographic characteristics and clinical parameters were recorded on a well-designed questionnaire. Ethical approval was obtained from the institutional research committee.

Biochemical Analysis

Fasting blood sample (5 mL) was collected from all the participants. It was centrifuged at 4500 rpm for 5 minutes to collect clear serum. Serum adiponectin, MDA, TAC, hs-CRP and vitamin D were determined with ELISA method.

Statistical Analysis

SPSS version 21 was used for statistical analysis. Variables were compared with independent student's t test. Association between adiponectin and other variables was carried out with Pearson's correlation co-efficient r. P value of less than 0.05 was considered significant.

Results

Table 1 shows the comparison of variables between the two study groups. Group A cases had 43 females and 17 males (72% F), group B controls had 18 males and 42 females (70% F). There was no significant difference between the ages of the two groups, almost 42 years means in both groups.

There was no significant difference in the BMI of the two groups (26.8 ± 3.4 vs 26.1 ± 3.1, p value 0.09). Furthermore, serum adiponectin (4.3±7.0 vs 9.4±5.5, P<0.0001) and vitamin D (17.06±6.4 vs 30.81± 3.3, P<0.0001) were found to be significantly lower in cases than control. The inflammatory marker hs-CRP (mg/L) and oxidative stress marker MDA (nmol/L) were significantly higher in patients with depression (4.4±2.7 vs 1.2 ±1.1) and (5.83±0.62 vs 2.52±0.84), P<0.0001). Table 2 shows Pearson correlation co-

efficient r value of adiponectin with other biochemical parameters. We observed that adiponectin correlated significantly positively with vitamin D (r 0.45, P<0.0001), and TAC (r 0.52, P<0.0001), and negatively with hs-CRP (r-0.33, P<0.0001) and MDA (r-0.38, P<0.0001).

Table 1: *Comparison of Biochemical Variables between Cases and Control*

Variables	Cases n=60 Means±SD	Control n=60 Means±SD	P-Value
Age (years)	42.4 ± 10.8	41.9 ± 11.6	0.80
BMI (kg/m^2)	26.8 ± 3.4	26.1 ± 3.1	0.09
hs-CRP (mg/L)	4.4±2.7	1.2 ±1.1	<0.001
MDA (nmol/L)	5.83±0.62	2.52±0.84	. <0.0001
Adiponectin (µg/mL)	4.3±7.0	9.4±5.5	<0.0001
Vitamin D (ng/mL)	17.06±6.4	30.81± 3.3	<0.0001)
TAC (U/mL)	24.50±3.9	34.17±4.6	<0.0001

Table 2: *Correlation of Adiponectin with Biochemical Parameters*

Variable	r	P value
Hs-CRP	-0.33	<0.0001
Vitamin D	0.45	<0.0001
MDA	-0.38	<0.0001
TAC	0.52	<0.0001

Discussion

In the present study we observed significantly lower levels of both adiponectin and vitamin D in patients with depression. The adiponectin levels correlated negatively with inflammatory marker (hs-CRP) and oxidative stress marker (MDA) while positively with vitamin D and Total Antioxidant Capacity. Adiponectin exerts anti-inflammatory effect which helps to protect against depression. Chronic low-grade inflammation is currently recognized as a central pathophysiological characteristic of depression, a meta-analysis confirmed increased inflammatory markers in depression (17). Adiponectin has been found to have neuroprotective role in studies performed on animals with adiponectin knock-out mice showing depressive behavior and reduced synaptic plasticity (18). Adiponectin modulates energy homeostasis and stress responses by activating adenosine monophosphate activated protein kinase (AMPK) pathway in the hypothalamus. Dysregulated AMPK signaling has been implicated in the pathophysiology of depression. Additionally, adiponectin improves insulin sensitivity; insulin resistance itself is associated with higher depression risk and poorer antidepressant response (19).

The low vitamin D observed in our study aligns with a meta-analysis of 25 observational studies (15) consisting of 49,231 patients concluding that low vitamin D doubles the odds of depressive disorder (OR=1.87). Vitamin D's association with depression is due to its role in: serotonin synthesis, neuronal plasticity in hippocampus, upregulation of antioxidant enzymes in brain and regulation of hypothalamic pituitary axis thus regulating cortisol secretion (20). Letho et al and Huang et al (21, 22) are the only previous studies that have examined both adiponectin and vitamin D in depressive disorder. Both found low adiponectin and vitamin D in their studies however Letho et al found no association of adiponectin with vitamin D. Our study is the first to demonstrate a significant correlation between the two identifying a possible synergistic role of both adiponectin and vitamin D in depressive disorders.

Conclusion

Adiponectin and vitamin D both were low in our patients with depression. Moreover, they associated inversely with inflammatory markers and oxidative stress markers. Future studies may implicate a potential combined therapeutic role of adiponectin and vitamin D supplements in these patients.

Strength

The strengths of our study include the selection of medication free cases, age, gender and BMI matched controls and the combined determination of adiponectin and vitamin D in the same study population.

Limitation

The cross-sectional study design with single-point collection of samples account for the limitation of our study.

Recommendation

Further research including prospective cohort and randomized controlled trials (RCTs) are recommended for future.

Conflict of Interest

None

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None

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