

Correlation of serum anti-müllerian hormone levels with serum follicular stimulating hormone, luteinizing hormone and testosterone levels in male patients of depression

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Abstract

Objective: To determine the correlation of serum anti-müllerian hormone with follicular stimulating hormone, luteinizing hormone and testosterone levels in male patients of depression.

Method: The cross-sectional analytical study was conducted at the Islamic International Medical College and the Armed Forces Institute of Mental Health, Military Hospital, Rawalpindi, Pakistan, from March 4, 2017, to March 29, 2018, and comprised male patients aged 18-60 years suffering from depression diagnosed on the basis of Siddiqui Shah Depression Scale. Serum anti-müllerian hormone, follicular stimulating hormone, luteinizing hormone and testosterone levels of all patients were measured using enzyme-linked immunosorbent assay kits. Correlation of anti-müllerian hormone with the rest was explored. Data was analysed using SPSS 21.

Results: There were 72 male subjects with mean age 35.19 ± 9.97 years. A significant negative correlation was observed between serum anti-müllerian hormone levels and serum follicular stimulating hormone levels ($p=0.001$), but the correlation was not significant with serum luteinizing hormone and serum testosterone levels ($p>0.05$).

Conclusion: Anti-Müllerian Hormone was found to be significantly correlated with follicular stimulating hormone, but not with luteinizing hormone and testosterone.

Key Words: Depression, Testosterone, Anti-müllerian hormone.

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Introduction

Depression is a state of low mood along with disturbances in biological and cognitive activities¹. It is a psychiatric illness with prevalence ranging from 3.7% to 4.3% in Pakistan². A variety of biological and social factors, such as genetic susceptibility, disrupted mood regulation by brain, medications, medical problems, familial environment, cultural norms, poor coping ability and stressful life events, can lead to the development of depression³. Chemical disturbances in levels of serotonin, cortisol, inflammatory mediators, vitamin D and neurotrophic factors also predispose an individual to depression⁴. It can compromise an individual's whole life by negatively affecting physical functioning, productivity and interpersonal relationships. It is also a major risk factor for many chronic conditions, like diabetes mellitus (DM), hypertension (HTN), stroke and cardiovascular events⁵. Depression can further complicate the management and worsen the severity of many chronic illnesses, including multiple types of cancer, Parkinson's disease and acquired immunodeficiency syndrome (AIDS)⁶.

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Studies have also determined the role of anti-müllerian hormone (AMH) in promoting normal brain development and cognition⁷. AMH is a glycoprotein synthesised by sertoli cells of testes in males, and granulosa cells of ovaries in females. In males, AMH levels are highest during infancy and then they gradually decline and maintain a certain level⁸. Regarding its effect in central nervous system (CNS), AMH promotes neuroserpin expression, neurogenesis as well as neuronal survival by acting on AMH receptors distributed in several brain regions, including the cortex, hippocampus and hypothalamus⁹. AMH is also capable of regulating the hypothalamic-pituitary-gonadal axis as AMH signalling pathway increases gonadotropin releasing hormone (GnRH) neuronal activity and secretion from hypothalamus, which is essential for optimal secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH). FSH increases AMH secretion through the FSH receptor (FSH-R) transduction pathway, and LH is responsible for the production of testosterone¹⁰⁻¹². Testosterone is involved in brain development and remodelling by enhancing synaptic connections, cell growth, cell migration, apoptosis and neurotransmitter metabolism, which results in the modulation of neuronal activity in the cortex¹³. Testosterone exerts a wide range of functions in males, which include the development of

secondary sexual characteristics, spermatogenesis and behavioural traits, like aggression, libido and sexual motivation¹⁴. Reduced sexual activity further complicates the severity and management of depression¹⁵. Thus, balanced AMH levels appear to have an important role in sexual activities and mental health of an individual¹⁶.

The relationship of AMH with gonadotropins and testosterone levels has not been extensively explored in male patients of depression. The current study was planned to fill the gap by estimating the correlation of serum AMH with FSH, LH and testosterone levels in male patients of depression.

Patients and Methods

The cross-sectional analytical study was conducted at the Islamic International Medical College and the Armed Forces Institute of Mental Health, Military Hospital, Rawalpindi, Pakistan, from March 4, 2017, to March 29, 2018, after approval from the ethics review committee of Riphah International University, Islamabad.

The sample size was calculated using Raosoft calculator¹⁷ by taking depression prevalence 4.2% at 95% confidence level and 5% standard error. After taking informed consent, participants were included by non-probability convenient sampling and they were male patients aged 18-60 years with depression diagnosed on the basis of Siddiqui Shah Depression Scale (SSDS), which is 36-item tool and each item is scored 0-4 with total score ranging 0-108. Scores of 26 or above are considered to be an indication of depression¹⁸. The subjects included had body mass index (BMI) <30 and had no physical deformity or chronic illness. Patients with BMI >30, undergoing electroconvulsive therapy (ECT), drug and alcohol abusers, and those suffering from chronic illness and obvious physical deformities were excluded.

Age and BMI of the participants were recorded and duration of depression was noted. Blood samples were taken and serum was separated after centrifugation of samples at 3000rpm for 10 minutes and stored at -20°C. Serum AMH (Ref # A79765) was estimated using enzyme-linked immunosorbent assay (ELISA) kit (Immunotech, Beckman Coulter, United States). Serum FSH (Cat # 10001), LH (Cat # 10004) and testosterone (Cat # 10007) levels were estimated using ELISA kit (Bioss, US).

Data was analysed using SPSS 21. Data was expressed as mean $\pm$ standard deviation (SD). Correlation of serum AMH with FSH, LH and testosterone levels was evaluated using Pearson correlation test. $P < 0.05$ was considered statistically significant.

Results

There were 72 male subjects with mean age 35.19 ± 9.97 years, mean BMI 23.85 ± 2.08 and mean depression duration 1.60 ± 1.43 years (Table 1).

Table-1: Mean values for age, body mass index (BMI), duration of illness, serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone and anti-müllerian hormone (AMH) in male patients with depression.

Parameter	Patients of Depression (n=72)
Age (years)	35.19 $\pm$ 9.97
Body Mass Index (BMI)	23.85 $\pm$ 2.08
Duration of illness (years)	1.60 $\pm$ 1.43
Serum FSH levels (mIU/ml)	3.32 $\pm$ 3.68
Serum LH levels (mIU/ml)	3.12 $\pm$ 1.60
Serum Testosterone levels (ng/ml)	8.92 $\pm$ 4.60
Serum AMH levels (ng/ml)	8.54 $\pm$ 5.26

AMH: Anti-müllerian hormone, FSH: Follicle stimulating hormone, LH: luteinizing hormone.

Table-2: Correlation of serum anti-müllerian hormone (AMH) level with serum follicle stimulating hormone (FSH), luteinizing hormone (LH) and testosterone level.

Serum AMH levels (ng/ml)	Serum FSH levels (mIU/ml)	Serum LH levels (mIU/ml)	Serum Testosterone levels (ng/ml)
	$r = -0.38^*$	$r = -0.05$	$r = 0.18$

Correlation of mean AMH levels (ng/ml) with mean FSH, LH and testosterone levels (ng/ml) was noted (Table 2).

A significant negative correlation was observed between serum AMH levels and serum FSH levels ($p=0.001$), but the correlation was not significant with serum LH and serum testosterone levels ($p>0.05$).

Discussion

The study showed that AMH was negatively correlated with FSH levels, which was also reported earlier¹⁹, but the study was conducted on infertile women with no depression. A study, conducted on testes of children and adolescents with disorders of the gonadal axis, demonstrated that serum AMH was informative about the functional capacity of the testicular tissue and it was also a reliable marker of FSH action in the prepubertal testis¹². Another study reported findings similar to those of the current study²⁰.

The current study showed no significant correlation of serum AMH levels with serum LH and serum testosterone levels. In a study conducted on normo-ovulatory women, a significant partial correlation between the serum LH/FSH ratio and AMH level was demonstrated, a finding which is contrary to the current study²¹. This contradiction could be

due to gender difference as reproductive hormones are under different regulatory mechanisms in males and females.

A study to find out relationship between AMH, testosterone, LH and FSH in men aged 30-75years who were on testosterone therapy showed that an increase in testosterone levels was associated with suppression of LH and FSH²². However, testosterone levels were not correlated with AMH, which is in accordance with the finding of the present study. In another study, it was observed that testosterone down-regulates AMH levels in bovine granulosa cells placed in culture²³. A study observed that AMH can be used as a marker for male fertility and, contrary to the current results, a significant positive correlation was found between serum AMH and testosterone levels in azoospermic men²⁴. Differences between results could be attributable to hypogonadism present in the earlier study.

Newly-diagnosed cases and a large sample size along with estimation of GnRH in male patients of depression would have been more effective, but these could not be done due to logistical and financial constraints, which is a limitation of the current study.

Patients suffering from depression without treatment may be included in further studies along with magnetic resonance imaging (MRI) for the analysis of hippocampal volume. In future, estimation of GnRH and neuroserpin may be considered along with AMH to have better understanding of hypothalamic pituitary testicular axis and neurogenesis in depression. Furthermore, additional studies are needed at the AMH receptor levels to clarify the effects of AMH.

Conclusion

Serum AMH was found to be correlated with FSH, but not with LH and testosterone in male patients of depression.

Disclaimer: The text is based on an M.Phil thesis.

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