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IMPACT OF OBESITY ON SERUM ANTI-MULLERIAN HORMONE LEVELS IN WOMEN OF REPRODUCTIVE AGE

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ABSTRACT

Background: This study was conducted to assess the impact of obesity on serum anti-mullerian hormone levels in women of reproductive age. **Material And Methods:** This was a prospective observational study conducted on 100 women belonging to the age group of 18-38 years. The study comprised of 2 groups of 50 women each with group A comprising obese women and group B comprising non-obese women. Body Mass Index (BMI) was calculated and women with BMI >25 Kg/m2 were considered obese. Serum Anti-Mullerian Hormone (AMH) levels were measured and compared between the two groups. Additionally, Waist Circumference (WC) and Waist-Hip Ratio (WHR) were measured to assess their association with decreased AMH levels. **Results:** The study revealed mean serum AMH levels of 2.87±1.55 ng/ml in obese and 3.55±1.34 ng/ml in non-obese women (p-value 0.0190). The mean AMH in women with higher waist circumference and higher WHR were 2.92±1.69 and 2.89±1.62 ng/ml respectively, which were less as compared to normal women. **Conclusion:** Mean serum AMH levels in obese women were lower as compared to non-obese women. Higher WC and the WHR were also found to be significantly related to low AMH levels.

KEYWORDS

obesity, low AMH, correlation, BMI, waist circumference

INTRODUCTION

Anti-Mullerian Hormone (AMH), also known as Mullerian Inhibiting Substance (MIS), is a key factor in embryonic sex differentiation in males. In postnatal females, AMH is secreted by primary, secondary and antral follicles and appears to regulate early follicular development.[1,2] The exact role of AMH in the ovary is not entirely clear, but the proposed functions include inhibition of follicular recruitment, inhibition of aromatase activity, and reduced sensitivity of follicles to FSH.[3,4]

AMH is a member of the transforming growth factor-β family. It is expressed in the granulosa cells of early-developing follicles in the ovary and is an inhibitor of follicular maturation and recruitment. AMH is emerging as an early predictor of ovarian reserve.[5-9] Serum AMH levels have been shown to decrease with age and serve as a stronger and more consistent indicator of ovarian ageing compared to the number of antral follicles, inhibin B, or FSH levels.[10] Women with Polycystic Ovarian Syndrome (PCOS) have 2- to 3-fold higher levels of AMH compared with healthy women. Clinically, AMH is used to predict outcomes with In-Vitro Fertilisation (IVF) as it is associated with the number of oocytes retrieved in an IVF cycle.[11-14] Obesity has been proposed as a factor that may reduce AMH levels. Obesity is associated with impaired ovarian reserve by impairing follicular development. It also disrupts hormonal balance through insulin resistance and chronic inflammation, further impacting ovarian reserve. The clinical implications include reduced fertility and decreased response to fertility treatment.[15]

This study was conducted to assess the impact of obesity on serum AMH levels in women of reproductive age.

MATERIAL AND METHODS

This prospective observational study included 100 women belonging to the age group of 18-38 years attending the Gynaecology OPD in Acharya Shri Chander College of Medical Science and Hospital, which is a tertiary care centre in Jammu region. Institutional Ethical Clearance was obtained to conduct the study. Women under 18 or over 38 years, as well as those with a history of endometriosis, polycystic ovarian syndrome, or previous chemotherapy or radiotherapy, were excluded from the study. The study comprised 2 groups of 50 women each with group A comprising of obese women and group B comprising of non-obese women. The Body Mass Index (BMI) of the subjects was calculated. Women with BMI > 25 Kg/m^2 were considered obese as per the WHO cutoffs for the Asian and South Asian populations.[16] Serum Anti-Mullerian Hormone levels were measured. Also, a correlation of AMH levels with obesity based on Waist Circumference (WC) was noted. As stated by WHO, WC>80 cm in women is associated with an increased risk of complications for Indian women. The Waist-Hip Ratio was also measured. A ratio of 0.85 or higher was considered the cutoff for obesity.[17] Mean and standard deviation were calculated for each group. Statistical analysis was conducted using SPSS software.

RESULTS:

In group A, the majority of women were in the age group of 18-25 years (46%) followed by 26-30 years (36%). In group B, 42% of women belonged to the age group of 18-25 years followed by 38% in the age group of 26-30 years **(Table 1).** Thus, the groups were comparable with respect to age. The mean serum AMH levels in obese women were 2.87±1.55 ng/ml, while in non-obese women, the mean was 3.55±1.34 ng/ml. A t-test yielded a t-statistic of -2.3835 and a p-value of 0.0190, indicating a statistically significant difference between the two groups. **(Table 2).** There was a statistically significant difference in mean AMH levels between women with waist circumference >80 cm (2.92 ± 1.69 ng/ml) and <80 cm (3.68 ± 1.56 ng/ml), t (98) = -2.4104, p = 0.0178 **(Table 3).** Similarly, a statistically significant difference was observed in mean AMH levels between women with waist-hip ratio >0.85 (2.89 ± 1.62 ng/ml) and <0.85 (3.59 ± 1.55 ng/ml), t (98) = -2.2452, p = 0.0269 **(Table 4).**

Table 1: Age-wise distribution of subjects

Age	Number of women in group A (n=50)	Number of women in Group B (n=50)
18-25 years	23 (46%)	21 (42%)
26-30 years	18 (36%)	19 (38%)
31-38 years	09 (18%)	10 (20%)

Table 2: Mean serum AMH levels in obese and non-obese women.

Groups	Mean serum AMH levels
Group A (Obese)	2.87 ± 1.55 ng/ml
Group B (Non-obese)	3.55 ± 1.34 ng/ml
t-value	-2.3835
p-value	0.0190

Table 3: Mean AMH levels based on waist circumference

Groups	Total women (n=100)	Mean AMH
WC >80	45	2.92 ± 1.69 ng/ml
WC <80	55	3.68 ± 1.56 ng/ml
t-value	-2.4104	
p-value	0.0178	

Table 4: Mean AMH levels based on waist-hip ratio

Groups	Total women (n=100)	Mean AMH
WHR > 0.85	47	2.89 ± 1.62 ng/ml
WHR < 0.85	53	3.59 ± 1.55 ng/ml
t-value	-2.2452	
p-value	0.0269	

DISCUSSION

AMH is secreted by small antral follicles, and elevated AMH levels in conditions such as polycystic ovarian syndrome reflect both an

increased number of these follicles due to a disturbance in the selection of the dominant follicle and an increase in production of AMH per granulosa cell, with the latter possibly related to intrinsic features of PCOS or an altered level of regulatory factors.[18,19]

Obesity is a major public health crisis in the United States.[20] More than two-thirds of the U.S. population is either overweight or obese.[21] BMI is one of the ways to measure obesity in the population. Other ways to measure obesity include the waist-to-hip ratio, the percentage of the body or visceral fat, and waist circumference.[22,23] BMI is typically used to assess the risk of developing chronic conditions such as diabetes, hypertension, depression, and cancer.[24] The BMI calculation falls within a numerical range, which places an individual into one of four categories. This data is used by researchers and physicians to educate patients and the public of potential health risks detected within a specified category.[25] Researchers continue to evaluate the correlation between BMI and long-standing illness as well as associations between waist circumference as a predictor of health.[26]

This study aimed to assess the impact of obesity on serum AMH levels. The study was done on a total of 100 women with an equal number of obese and non-obese women. The groups were comparable concerning age. The mean serum AMH levels in obese women were 2.87±1.55 ng/ml and the mean serum AMH levels in non-obese women were 3.55±1.34 ng/ml. Women with lower waist circumference (<80 cm) have significantly higher mean AMH levels (3.68 ng/ml) compared to women with higher waist circumference (2.92 ng/ml). Women with a lower waist-hip ratio (<0.85) have significantly higher mean AMH levels (3.59 ng/ml) compared to women with a higher waist-hip ratio (2.89 ng/ml). These findings throw light on the clinical use of these parameters in addition to BMI to correlate obesity with low AMH levels. However, BMI remains the standard and convenient method to measure obesity in the population.

Freeman EW et al[27] described AMH levels in healthy late reproductive-age women and tested the hypothesis that AMH levels are lower in obese compared to non-obese women. AMH levels were 65% lower in obese women compared to non-obese women (0.016 ng/mL and 0.046 ng/mL, respectively). BMI remained significantly associated with AMH levels in multivariable models that included adjustments for menopausal status, age, race and cycle day. In the longitudinal analysis of a subgroup, obese women had significantly lower mean AMH levels over the 8-year interval compared to the non-obese women (0.459 ng/mL; CI 0.28, 0.75 and 0.566 ng/mL; CI 0.34, 0.94, respectively; *P*=.016), corroborating the cross-sectional study results. Obese women have lower AMH levels compared to non-obese women in the late reproductive years. The findings offer further evidence of the complex relationships between obesity and reproductive hormone levels in women.

Moy V et al[28] determined the effect of obesity on serum AMH levels among women from different racial backgrounds. Age correlated negatively with AMH and antral follicle count across all races ($p < 0.05$). After adjusting for age, polycystic ovary syndrome diagnosis, and smoking, elevated BMI correlates negatively with AMH in Caucasian women but not in African-American, Hispanic, or Asian women. Additional studies are needed to elucidate further the effect of race on the interaction between obesity and ovarian reserve.

Lia A Bernardi[15] determined whether there is an association between obesity and Anti-Müllerian hormone (AMH) amongst reproductive-aged African-American women (AAW). Participants with obesity had AMH concentrations that were 23.7% lower than those with a BMI ≤ 25 kg/m^2 (2.9 ng/mL versus 3.8 ng/mL).

CONCLUSION

The study concludes that mean serum AMH levels in obese women were lower as compared to mean serum AMH levels in non-obese women. The waist circumference and the waist-hip ratio were also found to be good parameters to study relation of obesity to serum AMH levels. This study highlights the clinical relevance of using multiple parameters to define obesity and its implications on AMH levels to guide fertility treatments.

REFERENCES

1. A.L. Durlinger, J.A. Visser, A.P. Themmen. Regulation of ovarian function: the role of anti-Mullerian hormone. Reproduction, 124 (2002), pp. 1-619
2. R. Fanchin, N. Louafi, D.H. Mendez Lozano, N. Frydman, R. Frydman, J. Taieb. Per-follicle measurements indicate that anti-mullerian hormone secretion is modulated by the extent of follicular development and luteinization and may reflect qualitatively the ovarian follicular status. Fertil Steril, 84 (2005), pp. 7-173
3. N. Josso, N. di Clemente, L. Gouedard. Anti-Mullerian hormone and its receptors. Mol Cell Endocrinol, 179 (2001), pp. 25-32.
4. A.L. Durlinger, M.J. Gruijters, P. Kramer, B. Karels, T.R. Kumar, M.M. Matzuk, U.M. Rose, F.H. de Jong, J.T.J. Uilenbroek, J.A. Grootegoed, A.P. Themmen. Anti-Mullerian hormone attenuates the effects of FSH on follicle development in the mouse ovary. Endocrinology, 142 (2001), pp. 4891-4899.
5. A. de Vet, J.S. Laven, F.H. de Jong, A.P. Themmen, B.C. Fauser. Antimullerian hormone serum levels: a putative marker for ovarian aging. Fertil Steril, 77 (2002), pp. 357-362.
6. I.A. van Rooij, F.J. Broekmans, G.J. Scheffer, C.W. Looman, J.D. Habbema, F.H. de Jong, B.J. Fauser, A.P. Themmen, E.R. te Velde. Serum antimullerian hormone levels best reflect the reproductive decline with age in normal women with proven fertility: a longitudinal study. Fertil Steril, 83 (2005), pp. 979-987.
7. La Marca A, De Leo V, Giulini S, Orvieto R, Malmusi S, Giannella L, Volpe A. Anti-Mullerian hormone in premenopausal women and after spontaneous or surgically induced menopause. J Soc Gynecol Investig 2005;12:545–8.
8. van Rooij IA, Tonkelaar I, Broekmans FJ, Looman CW, Scheffer GJ, de Jong FH, Themmen AP, te Velde ER. Anti-mullerian hormone is a promising predictor for the occurrence of the menopausal transition. Menopause 2004;11:601–6.
9. Fanchin R, Schonauer LM, Righini C, Guibourdenche J, Frydman R, Taieb J. Serum anti-Mullerian hormone is more strongly related to ovarian follicular status than serum inhibin B, estradiol, FSH and LH on day 3. Hum Reprod 2003;18:323–7.
10. Piltonen T, Morin-Papunen L, Koivunen R, Perheentupa A, Ruokonen A, Tapanainen JS. Serum anti-Mullerian hormone levels remain high until late reproductive age and decrease during metformin therapy in women with polycystic ovary syndrome. Hum Reprod 2005;20: 1820–6.
11. Cook CL, Siow Y, Brenner AG, Fallat ME. Relationship between serum müllerian-inhibiting substance and other reproductive hormones in untreated women with polycystic ovary syndrome and normal women, Fertil Steril, 2002, vol. 77 (pg. 141-146)
12. Pigny P, Merlen E, Robert Y, Cortet-Rudelli C, Decanter C, Jonard S, Dewailly D. Elevated serum level of Anti-Mullerian Hormone in patients with polycystic ovary syndrome: relationship to the ovarian follicle excess and to the follicular arrest, J Clin Endocrinol Metab, 2003, vol. 88 (pg. 5957-5962)
13. La Marca A, Malmusi S, Giulini S, Tamaro LF, Orvieto R, Levratti P, Volpe A. Anti-Mullerian hormone plasma levels in spontaneous menstrual cycle and during treatment with FSH to induce ovulation, Hum Reprod, 2004, vol. a 19 (pg. 2738-2741)
14. Laven JSE, Mulders AGMGJ, Visser JA, Themmen AP, de Jong FH, Fauser BCJM. Anti-Mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age, J Clin Endocrinol Metab, 2004, vol. 89 (pg. 318-323)
15. Bernardi LA, Carnethon MR, de Chavez PJ, Ikhena DE, Neff LM, Baird DD, Marsh EE. Relationship between obesity and anti-Müllerian hormone in reproductive-aged African American women. Obesity (Silver Spring). 2017 Jan;25(1):229-235.
16. Weir CB, Jan A. BMI Classification Percentile And Cut Off Points. [Updated 2023 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan
17. KG Shruthi et al. Assessment of obesity in the Indian setting: A clinical review. Clinical epidemiology and global health.2023.Vol 23.101348
18. Visser JA, de Jong FH, Laven JSE, Themmen APN. Anti-Mullerian hormone: a new marker for ovarian function, Reproduction, 2006, vol. 131 (pg. 1-9)
19. Pellatt L, Hanna L, Brincat M, Galea R, Brain H, Whitehead S, Mason H. Granulosa cell production of anti-mullerian hormone is increased in polycystic ovaries, J Clin Endocrinol Metab, 2007, vol. 92 (pg. 240-245)
20. Comparative effectiveness of two popular weight loss programs in women I: body composition and resting energy expenditure. Mardock M, Lockard B, Oliver J, et al. https://jissn.biomedcentral.com/articles/10.1186/1550-2783-8-S1-P4 J Int Soc Sports Nutr. 2011;8:0.
21. Efficacy of a randomized trial examining commercial weight loss programs and exercise on metabolic syndrome in overweight and obese women. Baetge C, Earnest CP, Lockard B, et al. Appl Physiol Nutr Metab. 2017;42:216–227.
22. Public Health Considerations Regarding Obesity. Tiwari A, Balasundaram P. https://www.ncbi.nlm.nih.gov/books/NBK572122/ StatPearls. Treasure Island. 2022
23. Pathophysiology of obesity. Khanna D, Rehman A. https://europepmc.org/article/NBK/nbk572076 StatPearls. Treasure Island. 2022
24. Association between sex and body mass index as mediated by temperament in a nonclinical adult sample. Oniszczenko W, Stanisławiak E. Eat Weight Disord. 2019;24:291–298.
25. Effects of diet and exercise-induced weight loss in sedentary obese women on inflammatory markers, resistin, and visfatin. Khanna D, Baetge C, Simbo S, et al. http://article.scholarena.co/Effects-of-Diet-and-Exercise-Induced-Weight-Loss-in-Sedentary-Obese-Women-on-Inflammatory-Markers-Resistin-and-Visfatin.pdf J Nutr Obes. 2017;1.
26. The risk of chronic diseases in individuals responding to a measure for the initial screening of depression and reported feelings of being down, depressed, or hopeless. Khatib M, Badillo N, Kahar P, Khanna D. Cureus. 2021;13:0.
27. Ellen W. Freeman, Clarisa R. Gracia, Mary D. Sammel, Hui Lin, Lony Chong-Leong Lim, Jerome F. Strauss. Association of anti-mullerian hormone levels with obesity in late reproductive-age women. Fertility and Sterility. 2007;87(1):101-106.
28. Moy, V., Jindal, S., Lieman, H. *et al.* Obesity adversely affects serum anti-müllerian hormone (AMH) levels in Caucasian women. *J Assist Reprod Genet* **32**, 1305–1311 (2015).