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RESEARCH ARTICLE

Association of BMI and AMH in infertile women with and without polycystic ovarian disease

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ABSTRACT

Objective: Infertility and obesity are problems that have been on the rise in the past two decades. Anti-mullerian hormone (AMH) is a useful marker of ovarian reserve and is frequently estimated while treating infertility patients. Our study aims at evaluating the relationship between serum AMH levels and BMI in infertile patients with and without polycystic ovarian disease. **Methods:** This cross-sectional study was conducted on 200 women attending the OPD for infertility treatment from February 2019 to January 2020 at a semi urban hospital in India. All patients underwent gynaecological examination and basic infertility investigations including BMI calculation. Serum AMH levels were estimated for all patients. Women were divided into 2 groups - those with PCOD and without PCOD. **Results:** Mean overall AMH level was 4.86± 4.44 ng/ml. There was no significant correlation between BMI and AMH levels in the non PCOD group (r - 0.022, $p > 0.05$). However, in the PCOD group, there was inverse correlation between BMI and AMH levels which was significant (r - 0.285, $p< 0.05$). **Conclusion:** There is no significant correlation of BMI and AMH levels in infertile women without PCOD. However, in women with PCOD, there is significant inverse correlation of BMI with serum AMH levels.

Keywords: Infertility, antimullerian hormone, body mass index, polycystic ovarian disease.

The modern world, today, is grappling with a variety of problems. On one hand, we in a developing country like India, are struggling to keep our population at bay. On the other hand, problems like infertility are on the rise, especially in the affluent class. According to a study by the World Health Organisation (WHO), the prevalence of primary infertility in India is around 3.9 - 16.8 % which is primarily concentrated in the urban population [1].

There could be a variety of reasons contributing to the rising incidence of infertility like stress, advanced age of marriage and conception, unhealthy lifestyle and food habits etc; obesity being a major contributor. Obesity is a condition involving excessive body fat and body mass index (BMI) is the gold standard measure to categorise obesity. Calculation of BMI is easily done by measuring the height and weight and BMI is globally used to assess the severity of obesity. Women with BMI ≥ 25 kg/m² are termed as being overweight whereas women with BMI ≥ 30 kg/m² fall in the obese category [2]. Measurement and categorisation of obesity is also of primary importance as obesity has a detrimental effect on the entire body, predisposing to a lot of medical conditions like hypertension and diabetes being the most common. As far as the female reproductive system is concerned, obesity has been seen to impair folliculogenesis and oocyte development in the ovary [3].

Polycystic ovarian disease (PCOD) is a heterogenous endocrine disorder in women of reproductive age group with a wide spectrum of clinical features such as obesity, menstrual disorders and hyperandrogenism. It is one of the commonest endocrine disorders affecting women these days and affects 5- 10 % of the reproductive population [4].

The characteristic feature is the increase in the levels of luteinizing hormone (LH) and increased levels of androgens leading to subsequent anovulation.

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To measure the ovarian function and ovarian reserve, estimation of anti mullerian hormone (AMH) levels is a very useful test. Estimation of AMH levels is a very popular test in patients of infertility as it is an indicator of ovarian reserve, which in turn is an indirect index of the reproductive capacity of a woman. AMH is a glycoprotein, secreted by the granulosa cells in the ovary after puberty. It helps in the development of the ovarian follicle and in the maturation of the oocyte. The main function of AMH seems to be the inhibition of the follicle stimulating hormone (FSH) dependant selection process in the early stages of folliculogenesis [5]. It also reduces the number of LH receptors in the granulosa cells, which is also a FSH induced process. Since the level of this hormone is fairly constant throughout the menstrual cycle, this test need not be timed according to the menstrual calendar, adding to its convenience [6]. The normal levelof AMH is taken as 2-6.8 ng/ml. AMH levels decrease with advancing age. At menopause, AMH levels are undetectable. Fertility of women is usually graded according to AMH levels and women with AMH levels ≤ 1 ng/ml are said to have a poor ovarian reserve [7].

AMH levels are seen to be high in obese patients and a high BMI is a frequent feature of PCOD [8]. A logical deduction would be to expect a high AMH levels in women with PCOD where an increased number of small antral follicles would increase the secretion of AMH. Our aim was to observe and determine any relationship between BMI and serum AMH levels in patients coming for infertility treatment to our hospital, with a special focus on patients with PCOD.

Materials and methods

This study was a cross sectional study conducted on 200 women attending the infertility clinic at a semi urban hospital in India from February 2019 to January 2020. Informed consent was taken from all patients participating in the study. The study was conducted in accordance with the ethical standards of our institution and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Inclusion criteria -

All women coming for infertility treatment between the ages of 20-40 years were included in the study.

Exclusion criteria -

Patients less than 20 years and more than 40 years, patients with coexisting endocrine diseases such as thyroid dysfunction, hyperprolactinemia, cushing's syndrome, congenital adrenal hyperplasia, diabetes, history of ovarian surgery and premature ovarian failure (FSH level > 15 IU/ml) were excluded from this study. Couples with male factor infertility were also excluded from the study.

All patients underwent a baseline assessment including gynaecological history, general physical and gynaecological examination and basic infertility investigations, including a transvaginal ultrasound on the second day of the menstrual cycle. Serum antimullerian hormone levels were measured on the first visit irrespective of the day of the cycle. Blood samples were collected from the cubital vein. Then, after waiting for clot retraction, the sample was centrifuged at 2000 rpm for 5 minutes and the serum obtained was stored for assay at 2-8° C. AMH levels were measured in ng/ml using chemiluminescent immunoassay (CLIA). The same assay was used for all AMH samples collected.

Women were divided into 2 groups - those with PCOD (Group A) and without PCOD (Group B). Patients were diagnosed as having polycystic ovarian disease based on Rotterdam criteria i.e., meeting two of the following three criteria: oligo/anovulation, hyperandrogenism, or polycystic ovaries on ultrasound. Polycystic ovaries were defined as having ≥ 12 small antral follicles per ovary. BMI was calculated for all women by dividing the weight in kilograms by the height in square metres.

Our primary outcome was to establish a correlation between AMH levels and BMI in patients with PCOD and also evaluate this relationship in the non PCOD infertility population in our clinic.

The data is presented as mean± standard deviation. The correlation between BMI and AMH levels was examined using Spearman correlation coefficient test. The correlation coefficient assesses the measure of the strength and direction of the linear relationship between two variables. A p value of < 0.05 is considered significant.

Results

Group 1 comprised of 50 patients diagnosed with PCOD. Group 2 had 150 patients of infertility due to reasons other than PCOD; such as tubal factors, poor ovarian responders and unexplained infertility. Figure 1 shows the overall age distribution. The maximum numbers of patients belong to the age group of 25 – 30 years, followed by 31 – 35 years.

The mean age, BMI and AMH levels of both the groups can be seen in table 1. As seen the AMH levels are much higher in the PCOD group (group 1). Furthermore, there is an inverse relationship between BMI and AMH which is statistically significant in group1 ($r = -0.285$, $p = 0.044$). On

the other hand, there is no association between BMI and AMH levels in Group 2 (r = - 0.022, p > 0.05).

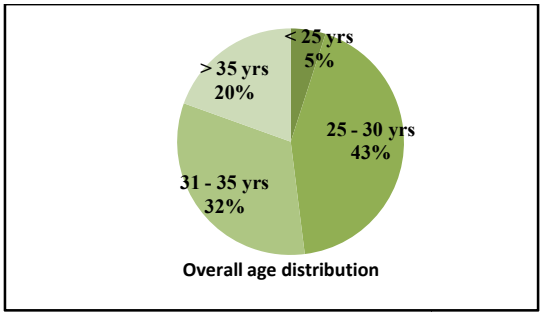

Figure 1: Overall age distribution

Figure 2 shows the proportion of lean PCOD patients (patients with BMI< 25) and non-lean PCOD (patients with BMI >25). As is seen a large proportion of patients are lean PCOD. The mean AMH level in this subgroup was 11.18 ± 2.64 ng/ml compared to 10.11 ± 4.26 ng/ml in the non-lean PCOD subgroup. However, this difference was not statistically significant (p > 0.05).

Table 1: Age, AMH and BMI values in both groups

Parameters	Group 1(n=50)			Group 2(n=150)			Overall
	Mean ± SD	r	P value	Mean ± SD	r	P value	Mean ± SD
AMH (ng/ml)	10.78±3.40	-0.285	0.044*	2.88±2.62	-0.022	0.793	4.86±4.44
BMI	24.32±4.62			23.17±3.17			23.46±3.60
Age	28.18±2.91			33.44±5.42			32.13±5.41

BMI - Body mass index, AMH - Anti mullerian hormone, SD - Standard deviation, *P < 0.05 is statistically significant.

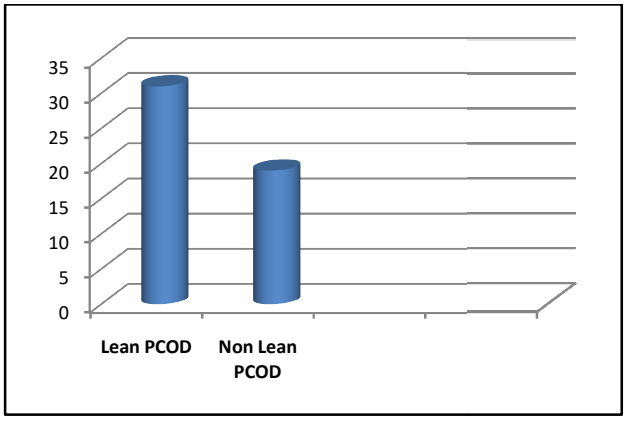

Figure 2: Distribution of lean PCOD and Non-lean PCOD.

Discussion

Obesity is a complex condition with multiple ramifications. It affects almost every function ofthe body, the reproductive system being no different. An increase in BMI results in impairment of the reproductive function by affecting the process of conception starting from folliculogenesis up to embryo development and implantation [9, 10].

The present existing studies show conflicting results. Freeman et al, in a study conducted on healthy women of late reproductive age group, found lower AMH levels in obese women as compared to non-obese women [11]. They also conducted a longitudinal analysis over a period of 8 years and found obese women to have lower AMH levels compared to women with normal BMI after making adjustments for other factors such as menopausal status, age, race etc.

In a similar study, Su et al found an inverse relationship between AMH levels and BMI in women of late reproductive age group. However, they also studied serum FSH and estradiol levels in these women and concluded that the decreased AMH levels were more a result of the physiological process than an actual decrease in ovarian reserve [8].

In our study, we had divided the women PCOD and non-PCOD groups. In the non-PCOD group, there was no significant correlation between BMI and serum AMH levels. This is consistent with the findings of Halawaty et al who studied the correlation of BMI and waist circumference (WC) in 3 types of ovarian reserve patterns - normal, high and poor ovarian reserve; and did not find any significant difference in these groups [12].

There was, however, a significant inverse relationship between AMH levels and BMI in the PCOD group. This can be explained due to the higher antral follicular count in PCOD women. A study by Piouka et al also demonstrated that AMH levels were inversely related to BMI and they concluded that estimation of serum AMH was a useful method of assessing the severity of PCOD [13].

The mean age in the non-PCOD group was 32.13 ± 5.41 years which was around 4 years more than the PCOD group and the mean AMH level was 2.88 ± 2.62 ng/ml which was lower than the PCOD group. This finding is consistent with the view that AMH levels decrease with age [14].

Our study group of PCOD women also had a significant proportion of women with normal BMI (≤ 25). These women, although not obese, showed other features of PCOD like anovulation and ultrasound confirmed polycystic ovaries. This category of PCOD patients is labelled as 'thin

polycystics' or lean PCOD. It has been seen that these patients may have higher levels of AMH as compared to obese PCOD and hence present a challenge to the clinician as they exhibit a poorer response to infertility treatment as compared to their obese counterparts [15,16]. In our study, although there was a difference in the mean AMH levels in the subgroups of patients with lean PCOD and obese PCOD, it was not proven to be statistically significant.

Limitations of our study include a discrepancy in the number of lean PCOD and non-lean PCOD patients. More studies need to be done for comparison between these two subgroups of PCOD patients. A better understanding is needed of the subgroup of lean PCOD to determine optimum treatment regimens to achieve a successful pregnancy. Also, measurement of FSH and LH levels was not included in the study, so the relationship between AMH and LH levels could not be studied.

Conclusion

To summarise, the current study could find no association between AMH levels and BMI in the general infertility female population; however, in women with PCOD, serum AMH levels are inversely related to BMI. The differences between the two subtypes of PCOD need further evaluation for better pregnancy outcomes.

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