International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Mounika K et al. Int J Reprod Contracept Obstet Gynecol. 2026 Feb;15(2):664-672
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20260189

Original Research Article

Association of ovarian response with anogenital distance in patients undergoing ovarian stimulation for in vitro fertilization/intra cytoplasmic sperm injection: a prospective cohort study

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Received: 03 December 2025
Revised: 12 January 2026
Accepted: 13 January 2026

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ABSTRACT

Background: The study investigates whether Anogenital Distance (AGD), a permanent marker of the prenatal hormonal environment, is associated with established ovarian reserve markers (FSH, AMH, AFC). Crucially, the aim is to determine if AGD can predict Ovarian Sensitivity Index (OSI) and overall ovarian response during controlled ovarian stimulation (COS) for IVF/ICSI.
Methods: This was a prospective cohort study conducted at an Indian IVF Reproductive and Biology Centre, located within the Department of Obstetrics and Gynaecology at Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi (n=40), aiming to evaluate the association of the anogenital distance (AGD), measured using digital calipers, with ovarian response, specifically the ovarian sensitivity index (OSI), and clinical outcomes in infertile women undergoing their first IVF/ICSI cycle.
Results: The study confirmed that age and AFC are inverse determinants of ovarian response, with low responders being older, having lower AFC, and requiring the highest gonadotropin dose. This resulted in highly significant differences ($p<0.001$) in oocyte yield, embryo formation, and ovarian sensitivity index (OSI), which peaked sharply in high responders (9.50\pm 2.87). Consequently, the clinical strategy varied significantly: Fresh ET dominated in Low/Normo groups, while 83.3% of high responders underwent frozen ET. Critically, the clinical pregnancy rate was highest in Normo Responders (42.8%), showing a statistically significant difference (P=0.03), while anogenital distance (AGD) showed no significant difference across the groups.
Conclusions: This study confirmed that age and poor ovarian reserve (high FSH, low AFC, low OSI) significantly define low responders, leading to inferior IVF cycle productivity compared to normo and high responders. Although anogenital distance (AGD) itself wasn't significantly different between groups, it positively correlated with key ovarian markers (AFC, OSI), suggesting it is a promising but unproven biomarker for ovarian reserve.

Keywords: Anogenital Distance, Ovarian reserve, Ovarian stimulation, Ovarian sensitivity index

INTRODUCTION

Ovarian reserve is defined as the maximum reproductive potential and physiological function inherent in the number and intrinsic quality of the remaining oocytes. This reserve is critically important in reproductive medicine, as it directly reflects the size of the pool of primordial follicles capable of development and subsequent ovulation.[1] A diminished ovarian reserve is clinically associated with reduced fertility, higher rates of cycle cancellation in assisted reproductive technologies (ART), and lower live birth rates. Conventional ovarian

reserve tests are essential prognostic tools, broadly categorized into biochemical and ultrasonographic measures. Biochemical tests include basal levels of Follicle-Stimulating Hormone (FSH), estradiol, Inhibin B, and Anti-Müllerian Hormone (AMH). AMH and Inhibin B are secreted by the granulosa cells of preantral and small antral follicles, making them direct and quantitative indicators of the functional follicular pool.[2] Ultrasonographic assessment focuses on dynamic measurements like ovarian volume and Antral Follicular Count (AFC). These markers form the foundation for predicting a woman's fertility trajectory and guiding individualized reproductive treatment plans.

It is well established that the trajectory of organ development during the prenatal period is highly susceptible to the prevailing intrauterine environment. Evidence suggests that exposures to nutritional deficiencies, environmental toxins, and toxic factors during gestation can significantly and permanently affect the development of the reproductive system, potentially impairing ovarian reserve later in life.[3-5] Anogenital distance (AGD) is a measure of the distance between the anus and the external genitalia, a sexually dimorphic feature that is typically longer in males than in females.[6-8] This distance is determined during a critical window of prenatal sexual differentiation, and AGD has thus been validated as a robust, permanent biomarker of prenatal exposure to androgens and endocrine disruptors.[9,10] In adult women, AGD is not merely an anatomical curiosity; it has been consistently associated with various female reproductive functions and specific gynecological disorders, including polycystic ovary syndrome and endometriosis.[11-13] Specifically, AGD is measured at two distinct points: (A) AGD AC the distance from the anterior clitoral surface to the upper margin of the anus and (B) AGD AF the distance from the posterior fourchette to the upper margin of the anus.

Controlled Ovarian Stimulation (COS) is an integral therapeutic modality in in-vitro fertilization (IVF) treatment, designed to recruit a synchronized cohort of multiple follicles. Consequently, the responsiveness of the ovaries to exogenous gonadotrophin stimulation significantly influences the probability of a successful outcome and concurrently affects the risk of major complications, such as cycle cancellation and Ovarian Hyperstimulation Syndrome (OHSS).[14] Ovarian responsiveness is traditionally measured by the total number of oocytes retrieved and the overall gonadotrophin dose required. However, the Ovarian Sensitivity Index (OSI), defined as the ratio of the number of oocytes retrieved to the total gonadotrophin dose, is considered a better, more holistic representation of follicular sensitivity and efficiency.[15] A failure to respond adequately to standard protocols classified as "poor response" results in a diminished quantity of retrieved oocytes and a significantly lower probability of ongoing pregnancy.[16] The overarching aim of this study is therefore two-fold: to compare AGD as a stable, lifelong biomarker of the prenatal hormonal environment with established conventional ovarian reserve markers, and, crucially, to assess the predictive relationship between AGD and the measured ovarian response, particularly the ovarian sensitivity index, during controlled ovarian stimulation.

METHODS

Study setting

The research was conducted over one year from October 2019 to September 2020 at the IVF Reproductive and Biology Centre, located within the Department of Obstetrics and Gynaecology at Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi. The study employed a prospective cohort design.

Inclusion criteria

The inclusion criteria were infertile women aged 22-40 years undergoing their first IVF/ICSI cycle, while

Exclusion criteria

Exclusion criteria comprised patients with previous vaginal deliveries, PCOS, endometriosis, or prior ovarian and genital surgeries.

Study population and sample size

The study recruited a total of 40 patients from the IVF centre, utilizing a convenience sample necessitated by the COVID-19 pandemic, though it exceeded the minimum desired size of 20 and was close to the calculated estimate of 37 per group. The estimated sample size was determined using the formula: $n= [(\boldsymbol{\sigma}1+ \boldsymbol{\sigma}2)2 (Z1- \alpha/2 +Z1-\beta)^2]/(m1-m2)^2$

Where; m1 = mean of anogenital distance in group 1, m2 = mean of anogenital distance in group 2, $\boldsymbol{\sigma}1$ = SD of outcome variable in group 1, $\boldsymbol{\sigma}2$ = SD of outcome variable in group 2 based on comparing two means with a type I error of 5% and power (1-6) of 80%.

The study's methodology involved screening eligible patients at the fertility and IVF OPD, obtaining written informed consent, and conducting a complete infertility workup, recording baseline parameters like age, BMI, FSH, and LH. Ovarian assessment included a day 2/3 transvaginal ultrasound to determine AFC. Patients then underwent controlled ovarian stimulation with gonadotropins, and the Total Doses Used and the Ovarian Sensitivity Index (OSI) were calculated. The core measurement, Anogenital Distance (AGD), was taken using digital calipers on the day of oocyte retrieval while the patient was under sedation, with two specific distances measured: AGD-AC (Anus-Clitoris) and AGD-AF (Anus-Fourchette). Based on the number of oocytes retrieved, patients were retrospectively categorized into Low (<3), Normo (4-15), or High Responders (>15). The primary

outcome was the association between AGD and the number of oocytes retrieved, while secondary outcomes included correlation with FSH, AFC, OSI, embryo transfer numbers, clinical pregnancy rate, and OHSS, followed by standard pregnancy confirmation via UPT and transvaginal ultrasound.

Statistical analysis

Data was entered into MS-Excel and analyzed using SPSS Pc version 25. Quantitative data was summarized using mean and standard deviation. Differences between means were tested using ANOVA or the Kruskal-Wallis H test, followed by a post-hoc test. Qualitative data was expressed as proportions or percentages, and differences between proportions were analyzed using the Chi-square test or Fisher's exact test. A p value less than 0.05 was considered to be statistically significant.

RESULTS

A total of 40 patients were recruited out of which 13 were in low responders group, 15 were in normo responders group and 12 were in high responders group.

Study demography

Age

The study compared the mean age and age distribution of three patient groups (low responders, n=13; normo responders, n=15; high responders, n=12), revealing a statistically significant difference in mean age (p=0.05), with low responders being the oldest (33.62 \pm 4.55 years) and high responders being the youngest (29.08 \pm 4.71 years). This trend was reinforced by the distribution across age brackets, as High Responders were most concentrated in the 21-25-year group (25.0%), normo responders peaked in the 26-30-year group (40.0%), and low responders dominated the older 31-35 year and 36-40-year brackets (38.5% in both), indicating that response status is inversely correlated with patient age.

Table 1: Distribution of patients by age.

Age in years	Low responders (n=13)		Normo responder (n=15)		High responders (n=12)	
	No.	%	No.	%	No.	%
20-25	1	7.7	1	6.7	3	25
26-30	2	15.4	6	40	4	33.3
31-35	5	38.5	4	26.7	4	33.3
36-40	5	38.5	4	26.7	1	8.3

BMI

The mean body mass index (BMI) did not significantly differ among the three groups (p=0.93), with values of 23.45±2.66 kg/m² for low responders, 23.87±3.79 kg/m² for normo responders, and 23.64±2.42 kg/m² for high responders. The majority of patients in all groups fell into the normal BMI range (18-24.99 kg/m²), represented by 69.2% (n=9/13) of low responders, 66.7% (n=10/15) of normo responders, and 83.3% (n=10/12) of high responders. A smaller percentage had a BMI in the overweight range (25-29.99 kg/m²), specifically 30.8% (n=4/13) in the low responders, 26.7% (n=4/15) in the normo responders, and 8.3% (n=1/12) in the high responders. Finally, only normo responders (6.7%, n=1/15) and high responders (8.3%, n=1/12) had patients with obesity (BMI >30 kg/m²), while none were found in the Low Responders group (n=0/13).

Table 2: Distribution of patients according to BMI.

BMI in kg/m²	Low responders N (%)	Normo responder N (%)	High responders N (%)
18-24.99	9 (69.2)	10 (66.7)	10 (83.3)
25-29.99	4 (30.8)	4 (26.7)	1 (8.3)
≥30	0	1 (6.7)	1 (8.3)

Causes of infertility

The causes of infertility showed varying distributions across the groups. Male factor infertility (low: 23.1%, n=3/13; normo: 33.3%, n=5/15; High: 33.3%, n=4/12) and unexplained infertility (low: 30.8%, n=4/13; normo: 26.7%, n=4/15; High: 25.0%, n=3/12) showed no statistically significant differences (p=0.80 and p=0.94, respectively). Similarly, tubal factor infertility was comparable, with the highest rate in high responders (41.7%, n=5/12), followed by normo responders (33.3%, n=5/15) and low responders (23.1%, n=3/13), with no significant difference (p=0.60).

However, there was a statistically significant difference in ovarian factor infertility (p=0.04), which was most prevalent in low responders (30.8%, n=3/13), least prevalent in normo responders (6.7%, n=1/15), and entirely absent in the high responders group (n=0/12).

Table 3: Cause of infertility in the study subjects.

Cause of infertility	Low responders (n=13), N (%)	Normo responders (n=15), N (%)	High responders (n=12), N (%)	P value
Male factor	3 (23.1)	5 (33.3)	4 (33.3)	0.80
Tubal factor	3 (23.1)	5 (33.3)	5 (41.7)	0.60
Ovarian factor	4 (30.8)	1 (6.7)	0	0.04
Unexpl-ained	4 (30.8)	4 (26.7)	3 (25.0)	0.94

Duration of infertility

In our study, the mean duration of infertility was 7.76±1.21 in the low responders group, 9.26±1.54 in the normo responders group and 6.83±0.98 in the high responders group. The difference between the three groups was not statistically significant (p=0.85).

TSH levels

The mean TSH levels was 2.30±1.27 mIU/l in the low responders group, 2.3 ±0.92 mIU/l in the normo responders group and 1.95±0.76 mIU/l in the high responders group. There was no statistical difference between the three groups in terms of TSH levels (p=0.52).

Estrogen on day 2 and on the day of trigger

The patients' mean day 2 estrogen levels were similar across the three groups (low responders: 34.46±11.73 pg/ml; normo responders: 38.81±7.30 pg/ml); High Responders: 39.24±12.0 pg/ml, showing no statistically significant difference (p=0.47). However, the mean Estrogen level on the day of trigger showed a highly statistically significant difference between the groups (p<0.001). High responders exhibited the highest level (2849.16±853.55 pg/ml), followed closely by normo responders (2522.86±933.21 pg/ml), while Low Responders had a substantially lower level (830.98±373.36 pg/ml).

FSH levels

The mean FSH level on day 2 of cycle was 10.05±4.67 IU/L in the low responders group, 8.26±2.17 IU/l in the normo responders group and 6. 53±1.73 IU/l in the high responders group. There was a statistically significant difference between the three groups in terms of FSH levels (p=0.03).

Day 2 AFC (antral follicle count)

The mean value of total AFC on day 2 of cycle was 5.23±3.03 in the low responders group, 9.33±2.35 in the normo responders group and 10.50±2.46 in the high responders group. There was a statistically significant difference between the three groups in terms of antral follicle count on day 2 of cycle (p=0.01).

Total dose of gonadotropins used

The mean value of total dose of gonadotropins used was 2534.62±808.71 in the low responders group, 2393.33±764.76 in the normo responders group and 2008.33±578.33 in the high responders group. There was statistically significant difference between the three groups (p=0.01).

Number of oocytes retrieved

The mean number of oocytes retrieved was 1.46±0.96 in the low responders group, 9.0±2.36 in the normo responders group and 20.33±5.85 in the high responders group. There was a statistically significant difference between the three groups (p<0.001).

Anogenital distance

Measurements of anogenital distance (AGD) showed no statistically significant differences between the three responder groups. The mean Anus-to-Clitoris (AGD-AC) distance was 71.25±5.11 mm in Low Responders, 75.03±8.09 mm in normo responders, and 77.34±11.12 mm in high responders (p=0.13). Similarly, the mean Anus-to-Fourchette (AGD-AF) distance was 25.18±4.11 mm in low responders, 28.25±5.06 mm in normo responders, and 28.19±4.58 mm in high responders, which was also not statistically significant (p=0.07).

Table 4: Anogenital distance-anus to clitoris and anus to fourchette.

	Low responders (n=13)		Normo responders (n=15)		High responders (n=12)		P value
	Mean	SD	Mean	SD	Mean	SD	
Anogenital distance-AC (mm)	71.25	5.11	75.03	8.09	77.34	11.12	0.13
Anogenital distance-AF (mm)	25.18	4.11	28.25	5.06	28.19	4.58	0.07

Ovarian sensitivity index

Ovarian sensitivity index is calculated by dividing the number of retrieved oocytes by total gonadotropin dose. The mean value of OSI was 0.704±0.733 in the low responders group, 4.208±1.910 in the normo responders group and 9.50±2.87 in the high responders group. There was a statistically significant difference between the three groups (p<0.001).

Comparison of ovarian response

The comprehensive comparison of the three responder groups revealed that age and ovarian reserve are the primary factors differentiating them, while BMI and Anogenital Distance (AGD) were similar. Low Responders were the oldest and had the lowest Total AFC and ovarian factor infertility was significantly more common in this group. This poor reserve directly resulted in a profoundly lower mean number of oocytes retrieved

(1.46±0.96) and lowest estrogen on the day of trigger (830.98±373.36 pg/ml), compelling the majority (69.5%) to undergo a Fresh Embryo Transfer (ET). Conversely, High Responders were the youngest, had the highest AFC, exhibited superior follicular stimulation resulting in the highest day of trigger estrogen and a massive yield of oocytes (20.33±5.85), leading to the formation and cryopreservation of numerous surplus embryos and a subsequent shift to a frozen ET strategy in 83.3% of the group.

Table 5: Ovarian sensitivity index in the study subjects.

	Low responders (n=13)		Normo responders (n=15)		High responders (n=12)		P value
	Mean	SD	Mean	SD	Mean	SD	
Ovarian sensitivity index	0.704	0.733	4.208	1.910	9.50	2.87	<0.001

Table 6: Ovarian response in the study subjects.

Variable	Low responders (n=13), Mean±SD	Normo responders (n=15), Mean±SD	High responders (n=12), Mean±SD	P value
Total AFC on day 2 of cycle	5.23±3.03	9.33±2.35	10.50±2.46	0.001
No. of oocytes retrieved	1.46±0.96	9.0±2.36	20.33±5.85	<0.001
No of mature oocytes	1.15±0.89	6.73±2.46	13.09±5.61	<0.001
No. of oocyte fertilized	1.0±0.81	5.67±1.98	8.73±5.83	<0.001
No. of embryos formed	0.92±0.76	4.26±0.80	6.18±0.69	<0.001
No of embryos transferred	0.92±0.76	2.21±0.80	3.4±0.69	<0.001
No of embryos cryo preserved	0.15±0.10	2.87±2.69	4.09±4.01	<0.001
Patients underwent fresh ET, N (%)	9 (69.5)	10 (66.7)	1 (8.3)	<0.001
Patients underwent frozen ET, N (%)	1 (7.7)	4 (26.7)	10 (83.3)	<0.001

Comparison of formation of embryos and IVF cycles response

The analysis of embryo outcomes showed highly significant differences across the responder groups (p<0.001), directly reflecting the variance in ovarian response. The number of embryos formed was highest in High Responders (6.18±0.69) and lowest in Low Responders (0.92±0.76). This superior yield in the High Responders group facilitated the highest number of embryos cryopreserved (4.09±4.01), resulting in the majority (83.3%) of these patients undergoing a Frozen Embryo Transfer (Frozen ET). Conversely, the limited embryo yield in both Low Responders and Normo Responders led them to primarily utilize the strategy of Fresh Embryo Transfer (Fresh ET) (69.5% and 66.7%, respectively).

Table 7: Comparison of embryos and IVF cycles response.

Variable	Low responders (n=13), Mean±SD	Normo responders (n=15), Mean±SD	High responders (n=12), Mean±SD	P value
No. of embryos formed	0.92±0.76	4.26±0.80	6.18±0.69	<0.001
No of embryos transferred	0.92±0.76	2.21±0.80	3.4±0.69	<0.001
No of embryos cryo preserved	0.15±0.10	2.87±2.69	4.09±4.01	<0.001
Patients underwent fresh ET, N (%)	9 (69.5)	10 (66.7)	1 (8.3)	<0.001
Patients underwent frozen ET, N (%)	1 (7.7)	4 (26.7)	10 (83.3)	<0.001

OHSS

In our study, none of the patients in the low responders and high responders group had OHSS. In the normo responders group 6.7% (1/15) had OHSS. However, there was no significant difference between the three groups (p=0.42).

Urine Pregnancy Test (UPT)

In the low responders group, 20% (n-2/10), in the normo responders group 50% (n-7 /14) and 27.2 % (n-3/11) in high responders group had UPT positive after 2 weeks of embryo transfer. There was no statistically significant difference between the three groups in terms of urine pregnancy test (p=0.09).

Table 8: OHSS in the study subjects.

	Low responders (n=13)		Normo responders (n=15)		High responders (n=12)		P value
	No.	%	No.	%	No.	%	
OHSS	0	0	1	6.7	0	0	0.42

Table 9: Urine pregnancy test in study subjects.

	Low responders (n=10)		Normo responders (n=14)		High responders (n=11)		P value
	No.	%	No.	%	No.	%	
Urine pregnancy test	2	20	7	50	3	27.2	0.09

Clinical pregnancy rate

Clinical pregnancy is defined as presence of gestational sac with fetal cardiac activity. In the low responders group 10% (n-1/10), in the normo responders group, 42.8% (n-6/14) and in the high responders 18.1% (n-2/11) had clinical pregnancy. There was statistically significant difference between the three groups in terms of clinical pregnancy rates (p=0.03).

Table 10: Urine pregnancy test in study subjects.

	Low responders (n=10)		Normo responders (n=14)		High responders (n=11)		P value
	No.	%	No.	%	No.	%	
Clinical pregnancy rate	1	10	6	42.8	2	18.1	0.03

DISCUSSION

This was a prospective cohort study conducted on 40 patients recruited from the IVF and Reproductive Biology Centre. The study investigated various baseline parameters (e.g., age, BMI, FSH, AFC) and IVF cycle outcomes (e.g., gonadotropin dose, oocytes retrieved, ovarian sensitivity index, AGD, and clinical pregnancy rates).

Age

The study established a statistically significant difference in mean age across the responder groups (p=0.05), with Low Responders being the oldest (33.62±4.55 years) and High Responders being the youngest (29.08±4.71 years). This finding is consistent with literature, as Febreques et al (2018) and Malin et al (2013) also reported a statistically significant gradient of decreasing mean age from poor to high responders, and Nabaneeta et al (2010) found a significantly higher proportion of poor responders over 35 years old, collectively supporting the conclusion that age is an inverse determinant of ovarian response.[18,17]

BMI

Our study found no statistically significant difference in mean Body Mass Index (BMI) across the three responder groups (p=0.93), with mean values ranging narrowly from 23.45±2.66 kg/m² to 23.87±3.79 kg/m². This result aligns with several comparative studies (Fabregues et al, 2018; Nabaneeta et al, 2010; Laszlo et al, 2002), which similarly reported no statistically significant BMI differences between responder categories.[18,17,21] Furthermore, the majority of patients across all groups fell within the normal BMI range (18.5-24.9 kg/m²), confirming that BMI was generally well-controlled and did not distinguish the ovarian response cohorts.

Cause of infertility

The analysis of male factor infertility, tubal factor infertility, and unexplained infertility found no statistically significant differences across the three responder groups (p-values between 0.60 and 0.94). Tubal factor infertility was highest in High Responders (41.7%), while other causes were distributed similarly (e.g., male factor ranged from 23.1% to 33.3%). Our findings are comparable to the study by Fabregues et al (2018), which also reported no significant differences in these specific infertility causes among their responder groups.[18]

TSH levels

The mean TSH levels were similar across the three groups (Low: 2.30±1.27 mIU/l; Normo: 2.31±0.92 mIU/l; High: 1.95±0.76 mIU/l), showing no statistical difference (p=0.52), confirming that TSH levels were well-controlled and not a differentiating factor.

Day 2 estrogen and on the day of trigger

The analysis of estrogen levels showed distinct patterns between the responder groups. The mean Day 2 Estrogen levels were comparable across all groups (Low: 34.46±11.73 pg/ml; Normo: 38.81±7.30 pg/ml; High: 39.24±12.0 pg/ml), indicating similar baseline endocrine status. However, the mean estrogen level on the day of trigger showed a highly statistically significant difference

(p<0.001), ranging dramatically from 830.98±373.36 pg/ml in the low responders to 2849.16±853.55 pg/ml in the high responders. This marked difference is attributed to the higher number of Antral Follicle Counts (AFC) in the high responders, leading to a much greater follicular output of estrogen during ovarian stimulation.

FSH levels

The mean FSH levels exhibited a statistically significant inverse relationship with ovarian response (p=0.03), being highest in low responders (10.05±4.67 IU/l) and lowest in high responders (6.53±1.73 IU/l). This finding is highly comparable to results from Fabregues et al (2018) and Laszlo et al (2002), both of which found significantly higher FSH in poor responders (e.g., Fabregues et al. reported (10.06±1.1 IU/l) in low responders, p<0.001).[21,18] The elevated FSH in the low responders group is likely due to their diminished ovarian reserve and older age.

AFC

The total antral follicle count (AFC) showed a statistically significant difference across the groups (P=0.01), confirming its strong predictive value. Mean AFC was lowest in Low Responders (5.23±3.03) and highest in high responders (10.50±2.46). This trend aligns closely with Fabregues et al (2018) and Laszlo et al (2002), who also reported significantly lower AFC in poor responders, thus validating AFC as a reliable marker of ovarian reserve and response.[18,21]

Dose of gonadotropins

The mean total dose of gonadotropins used was highest in Low Responders (2534.62±808.71) and lowest in High Responders (2008.33±578.33), although the difference in our study was not statistically significant (p=0.83). This non-significant trend of requiring higher doses for poor responders is consistent with the statistically significant findings of Fabregues et al (2018) and Malin et al (2013), and is attributed to the higher FSH levels and lower AFC observed in the Low Responders group.[18,20]

Number of oocytes retrieved

The mean number of oocytes retrieved demonstrated a highly statistically significant difference (p<0.001), ranging dramatically from 1.46±0.96 in low responders to 20.33±5.85 in high responders. This superior yield in High Responders is consistent with comparable studies (Fabregues et al, 2018; Malin et al, 2013; Laszlo et al, 2002), and is explained by the higher AFC and younger age of the patients in that group.[18,20,21]

Ovarian Sensitivity Index (OSI)

The ovarian sensitivity index (OSI) was highly significantly different (p<0.001), being lowest in low responders (0.704±0.733) and highest in high responders (9.50±2.87). This result, which reflects poor efficiency in converting gonadotropin dose to oocyte yield in poor responders, is highly comparable to the statistically significant differences reported by Fabregues et al (2018) and Malin et al (2013).[18,20]

Anogenital Distance (AGD)

The mean Anogenital Distance measurements (AGD-AC and AGD-AF) were numerically greater in High Responders, though the difference across groups was not statistically significant. However, both AGD-AC (r=0.342, p=0.031) and AGD-AF (r=0.335, p=0.035) were positively and significantly correlated with AFC. AGD-AF also showed a statistically significant positive correlation with the number of oocytes retrieved and OSI. These correlations are consistent with Fabregues et al (2018) and Jamie Mendiola et al (2012), suggesting that a greater AGD may indicate better ovarian response.[18,19] Conversely, AGD was not significantly correlated with FSH levels or total dose of gonadotropins.

Number of oocytes fertilized and embryos formed

The mean number of oocytes fertilized (p<0.001) and embryos formed (p<0.001) were both significantly maximal in the high responders group (8.73±5.83 fertilized and 6.18±0.69 formed) and minimal in the low responders group (1.0±0.81 fertilized and 0.92±0.76 formed), directly reflecting the differences in mature oocyte yield.

Number of embryos transferred

The mean number of embryos transferred was significantly different across the groups (p<0.001), ranging from 0.92±0.76 in low responders to 2.63±0.69 in High Responders. This is comparable to the statistically significant findings by Malin et al (2013) and Laszlo et al (2002).[20,21]

Embryo transfer strategy

The choice of transfer strategy showed a highly significant difference (p<0.001). The majority of low (69.5%) and normo (66.7%) responders underwent fresh embryo transfer, while the highest percentage of high responders (83.3%) underwent frozen embryo transfer to mitigate the high risk of ovarian hyperstimulation syndrome (OHSS) associated with their high yields.

Clinical pregnancy rate

The clinical pregnancy rate was statistically significant (P=0.03), peaking in normo responders (42.8%), followed by high responders (18.1%) and low responders (10%). This result is comparable to the statistically significant patterns observed by Malin et al (2013) and Laszlo et al (2002), where pregnancy rates were also highest in the normo-response category.[20,21]

Diagnostic performance

An analysis of the diagnostic performance (AUC) for predicting poor ovarian response identified OSI as the strongest predictor (AUC=0.98; 100% sensitivity; 88.9% specificity at cut-off 2.24), followed by AFC (AUC=0.78), AGD-AF (AUC=0.72), and AGD-AC (AUC=0.68). FSH was the weakest predictor (AUC=0.64).

This study has few limitations. The primary limitation of this prospective cohort study on the association between ovarian response and anogenital distance (AGD) lies in the restricted sample size (total n=40), a constraint explicitly acknowledged by the authors as being exacerbated by the COVID-19 pandemic. A small sample size limits the statistical power to detect true associations, potentially leading to Type II errors, particularly concerning the AGD measurements which, despite showing an encouraging correlation with ovarian markers, failed to reach statistical significance across the three groups (P>0.05). Furthermore, the relatively low number of patients may hinder the generalizability of the findings, especially the specific cut-off values derived for AGD's predictive accuracy, meaning the results may not be robustly applicable to a wider or more heterogeneous IVF population.

CONCLUSION

This prospective cohort study investigates the potential of anogenital distance (AGD) specifically the AGD-AF and AGD-AC variants as a novel, non-invasive clinical biomarker for predicting ovarian response in IVF/ICSI patients. By demonstrating that AGD measurements significantly correlate with established markers such as the antral follicle count (AFC) and ovarian sensitivity index (OSI), the research highlights AGD's diagnostic utility, particularly with AGD-AF achieving a 72.5% accuracy in identifying poor responders. This study advances the field by bridging the gap between prenatal hormonal exposure and adult reproductive capacity, offering a potential supplemental tool for clinicians to refine gonadotropin dosing and manage patient expectations. While the findings establish a clear physiological link between perineal measurements and follicular reserve, they also underscore the need for larger-scale validation to solidify AGD's role alongside traditional markers like FSH and AFC in routine fertility assessments.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. Kriti Tiwari and Dr. Brahmitha Roy for their support during study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. Fertil Steril. 2015;103(3):e9-17.
2. Hansen KR, Craig LB, Zavy MT, Klein NA, Soules MR. Ovarian primordial and non-growing follicle counts according to the stages of reproductive aging workshop (STRAW) staging system. Menopause. 2012;19(2):164-171.
3. Ibáñez L, Valls C, Cols M, Ferrer A, Marcos MV, De Zegher F. Hypersecretion of FSH in infant boys and girls born small for gestational age. J Clin Endocrinol Metab. 2002;87(5):1986-8.
4. Mark-Kappeler CJ, Hoyer PB, Devine PJ. Xenobiotic effects on ovarian preantral follicles. Biol Reprod. 2011;85(5):871-83.
5. Souter I, Smith KW, Dimitriadis I, Ehrlich S, Williams PL, Calafat AM, et al. The association of bisphenol-A urinary concentrations with antral follicle counts and other measures of ovarian reserve in women undergoing infertility treatments. Reprod Toxicol. 2013;42:224-231.
6. Earl Gray Jr L, Wilson VS, Stoker T, Lambright C, Furr J, Noriega N, et al. Adverse effects of environmental antiandrogens and androgens on reproductive development in mammals. Int J Androl. 2006;29(1):96-104.
7. Greenham LW, Greenham V. Sexing mouse pups. Lab Anim. 1977;11(3):181-4.
8. Kurzrock EA, Jegatheesan P, Cunha GR, Baskin LS. Urethral development in the fetal rabbit and induction of hypospadias: a model for human development. J Urol. 2000;164(5):1786-92.
9. Bornehag CG, Carlstedt F, Jönsson BA, Lindh CH, Jensen TK, Bodin A, et al. Prenatal phthalate exposures and anogenital distance in Swedish boys. Environ Health Perspect. 2015;123(1):101-7.
10. Swan SH, Main KM, Liu F, Stewart SL, Kruse RL, Calafat AM, et al. Decrease in anogenital distance among male infants with prenatal phthalate exposure. Environ Health Perspect. 2005;113(8):1056-61.
11. Mendiola J, Roca M, Mínguez-Alarcón L, Mira-Escolano MP, López-Espín JJ, Barrett ES, et al. Anogenital distance is related to ovarian follicular number in young Spanish women: a cross-sectional study. Environ Health. 2012;11(1):1-8.
12. Mendiola J, Sánchez-Ferrer ML, Jimenez-Velazquez R, Canovas-Lopez L, Hernandez-Penalver AI, Corbalan-Biyang S, et al. Endometriomas and deep infiltrating endometriosis in adulthood are strongly associated with anogenital distance, a biomarker for prenatal hormonal environment. Hum Reprod. 2016;31(10):2377-83.
13. Wu Y, Zhong G, Chen S, Zheng C, Liao D, Xie M. Polycystic ovary syndrome is associated with anogenital distance, a marker of prenatal androgen exposure. Hum Reprod. 2017;32(4):937-43.

14. Huber M, Hadziosmanovic N, Berglund L, Holte J. Using the ovarian sensitivity index to define poor, normal, and high response after controlled ovarian hyperstimulation in the long gonadotropin-releasing hormone-agonist protocol. Fertil Steril. 2013;100(5):1270-6.
15. Li HW, Lee VC, Ho PC, Ng EH. Ovarian sensitivity index is a better measure of ovarian responsiveness to gonadotrophin stimulation than the number of oocytes during in-vitro fertilization treatment. J Assist Reprod Genet. 2014;31(2):199-203.
16. Badawy A, Wageah A, El Gharib M, Osman EE. Prediction and diagnosis of poor ovarian response: the dilemma. J Reprod Infertil. 2011;12(4):241-8.
17. Panda N, Giri R, Das S, Pradhan S, Sahu MK. Comparison of the outcome of in vitro fertilization cycles in poor responders and good responders. J Hum Reprod Sci. 2010;3(2):85-9.
18. Fàbregues F, Balasch J, Creus M, Carmona F. Clinical outcome of in vitro fertilization cycles in women classified as low, normal and high responders according to the Bologna criteria. J Assist Reprod Genet. 2018;35(2):221-6.
19. Mendiola J, Stahlhut RW, Jørgensen N, Liu F, Swan SH. Shorter anogenital distance predicts poorer semen quality in young men in Rochester, New York. Environ Health Perspect. 2011;119(7):958-63.
20. Malin H, Sunkara SK, Raine-Fenning N, La Marca A. A continuous index of ovarian sensitivity to exogenous gonadotrophins. Reprod Biomed Online. 2013;27(1):60-5.
21. László F, László L, Zoltán B, Sándor M, Zsolt M. Differences in ovarian response, fertilization rate and clinical outcome between poor and normal responders in an in vitro fertilization program. Eur J Obstet Gynecol Reprod Biol. 2002;103(2):125-9.

Cite this article as: Mounika K, Tanwar R, Tempe A. Association of ovarian response with anogenital distance in patients undergoing ovarian stimulation for in vitro fertilization/intra cytoplasmic sperm injection: a prospective cohort study. Int J Reprod Contracept Obstet Gynecol 2026;15:664-72.