Effect of Metformin on Anti-Mullerian Hormone Level in Infertile Women with Polycystic Ovary Syndrome

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder and major cause of anovulatory infertility, often associated with metabolic dysfunction. Anti-Mullerian hormone (AMH), typically elevated in PCOS, may be modulated by metformin therapy, though existing evidence remains inconsistent. **Objective:** The aim of the study was to evaluate the effect of metformin on serum Anti-Mullerian Hormone levels in infertile women with Polycystic Ovary Syndrome. **Methods & Materials:** This prospective interventional study at the Department of Obstetrics and Gynaecology, Bangladesh Medical University (BMU), Dhaka, Bangladesh, from January to December 2025, included 80 infertile women with PCOS. Participants received three months of oral metformin, and serum AMH was measured pre- and post-treatment. Demographic and clinical data were collected, and AMH changes, BMI-stratified effects, and correlations with baseline AMH were analyzed using SPSS 25.0 ($p < 0.05$). **Results:** Among 80 infertile women with PCOS (mean age 29.1 ± 4.5 years), most were overweight or obese (65.0%), with menstrual irregularity in 72.5% and hyperandrogenism in 65%. Baseline AMH was 8.4 ± 2.1 ng/mL and decreased to 6.1 ± 1.8 ng/mL after 3 months of metformin (mean reduction 2.3 ± 1.2, $p < 0.001$), with 77.5% showing a decrease. AMH reduction was greatest in obese participants, and baseline AMH positively correlated with BMI ($r = 0.41$) and AMH reduction ($r = 0.52$), all $p < 0.001$. **Conclusion:** Metformin effectively reduces elevated serum AMH levels in infertile women with PCOS, with greater reductions observed in those with higher BMI.

Keywords: *Polycystic Ovary Syndrome, Metformin Therapy, Anti-Mullerian Hormone.*

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INTRODUCTION

Polycystic ovary syndrome (PCOS) represents a leading cause of endocrine disorders and anovulatory infertility in women. Affecting approximately 5% to 10% of women, it stands as the most frequently encountered gynecological endocrine condition among adolescents and women of reproductive age [1]. The syndrome is defined by three primary features: hyperandrogenism (HA), ovulatory dysfunction (OD), and polycystic ovarian morphology (PCOM), with the diagnosis requiring the presence of at least two of these criteria [2]. Women with PCOS frequently experience reproductive complications, including irregular menstrual cycles and infertility, which often drive them to seek medical attention. Beyond reproductive challenges, PCOS is associated with multiple metabolic disturbances, placing affected women at higher risk for insulin resistance, impaired glucose metabolism, dyslipidemia, and increased susceptibility to cardiovascular disease [2].

Anti-Mullerian hormone (AMH) is a dimeric glycoprotein that belongs to the transforming growth factor B (TGF-B) family and is produced exclusively by the granulosa cells of primary, preantral, and small antral ovarian follicles. The serum levels of AMH reflect the size of the ovarian follicular pool. In women, AMH secreted from antral and small antral follicles plays an essential role in the early recruitment of follicles, their growth, selection of dominant follicles, and final maturation during folliculogenesis [3]. Studies have shown that women with PCOS have serum AMH concentrations two to three times higher than those of healthy women. Compared with other markers such as inhibin, estradiol, or follicle-stimulating hormone, AMH is considered a more reliable indicator of ovarian function and follicular reserve [4]. In addition, AMH acts in a paracrine manner within the ovary, independent of gonadotropin signaling, with its levels closely reflecting the number of small antral follicles present.

Metformin, a widely used antihyperglycemic agent, has been introduced as a therapeutic option for women with PCOS. Evidence indicates that metformin can restore regular menstrual cycles and enhance ovulatory function in affected women. Recognized as a primary treatment for insulin resistance, metformin improves insulin sensitivity, reduces androgen levels, and promotes normalization of ovulatory cycles. Its clinical benefits in PCOS include regulation of menstrual cycles, induction of ovulation, and improved fertility potential [5]. These effects are thought to occur through increased hepatic production of sex hormone-binding globulin (SHBG), reduced adrenal and ovarian androgen secretion, and enhanced ovarian responsiveness [6]. Given the role of insulin resistance in PCOS and the associated elevation in AMH, metformin has been hypothesized to mitigate insulin resistance and thereby influence AMH levels in these women [7,8].

Despite this, the effect of metformin on serum AMH concentrations in women with PCOS remains uncertain [9]. Research findings are inconsistent, with some studies demonstrating reductions in AMH following metformin therapy, while others report no significant changes [10]. Nonetheless, improvements in metabolic parameters such as body weight and insulin sensitivity may indirectly benefit reproductive function. Furthermore, there is a lack of comprehensive systematic reviews or meta-analyses assessing the effects of metformin on AMH, particularly within specific populations, including women in Bangladesh. This highlights the need for further research to evaluate the effect of metformin on serum Anti-Mullerian Hormone levels in infertile women with Polycystic Ovary Syndrome.

Objective

To evaluate the effect of metformin on serum Anti-Mullerian Hormone levels in infertile women with Polycystic Ovary Syndrome.

METHOD & MATERIALS

This prospective interventional study was conducted at the Department of Obstetrics and Gynaecology, Bangladesh Medical University (BMU), Dhaka, Bangladesh, from January to December 2025. A total of 80 infertile women diagnosed with Polycystic Ovary Syndrome (PCOS) were enrolled to evaluate the effects of metformin therapy on serum Anti-Mullerian Hormone (AMH) levels.

Inclusion Criteria:

- Women diagnosed with PCOS based on the Rotterdam criteria.
- Infertile women seeking treatment for conception.
- Age between 20 and 40 years.
- Willingness to participate and provide informed consent.
- Baseline serum AMH measurement available before starting metformin therapy.

Exclusion Criteria:

- Women with other endocrine disorders (e.g., thyroid dysfunction, hyperprolactinemia, Cushing's syndrome).
- History of ovarian surgery or pelvic inflammatory disease.
- Current use of hormonal medications or insulin sensitizers other than metformin.
- Pregnant or lactating women.
- Known hypersensitivity to metformin.
- Severe hepatic, renal, or cardiovascular disease.

Participants were enrolled using purposive sampling, and the diagnosis of PCOS was confirmed according to the Rotterdam criteria, requiring at least two of the following: oligo/anovulation, clinical and/or biochemical hyperandrogenism, or polycystic ovarian morphology on ultrasound. Baseline demographic and clinical data, including age, body mass index (BMI), menstrual pattern, presence of clinical hyperandrogenism, and duration of infertility, were recorded. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²) and categorized according to WHO criteria.

All participants received oral metformin at standard therapeutic doses for three months while maintaining their usual diet and physical activity. Serum AMH levels were measured at baseline and after 3 months using a standardized enzyme-linked immunosorbent assay (ELISA). The primary outcome was the change in serum AMH levels following metformin therapy, while secondary outcomes included the proportion of participants showing decreased, unchanged, or increased AMH, stratified AMH changes according to BMI, and correlations between baseline AMH, BMI, and magnitude of AMH reduction.

Data were analyzed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency and percentage. Paired t-tests were used to compare pre- and post-treatment AMH levels. Stratified analyses were performed according to BMI categories, and Pearson correlation coefficients assessed associations between baseline AMH, BMI, and AMH reduction. A p-value < 0.05 was considered statistically significant. Written informed consent was obtained from all participants, and confidentiality was maintained throughout the study.

RESULTS

Table I shows the baseline demographic and clinical characteristics of the 80 infertile women with polycystic ovary syndrome. The majority of participants were aged 26–30 years (36/80, 45.0%), followed by 31–35 years (20/80, 25.0%), 20–25 years (16/80, 20.0%), and >35 years (8/80, 10.0%). Regarding BMI, 37 participants (46.2%) were overweight, 23 (28.8%) were obese, and 20 (25.0%) had normal weight. Menstrual irregularity was present in 58 participants (72.5%), and clinical hyperandrogenism was observed in 52 participants (65%). The mean duration of infertility was 3.2 ± 1.4 years, and the baseline serum AMH level was 8.4 ± 2.1 ng/mL.

Table I
Baseline Demographic and Clinical Characteristics of Study Participants (n = 80).

Variable		Frequency (n)	Percentage (%)
Age Group (years)	20–25	16	20.0
	26–30	36	45.0
	31–35	20	25.0
	>35	8	10.0
	Mean ± SD (years)	29.1 ± 4.5	
BMI Category	Normal (18.5–24.9)	20	25.0
	Overweight (25–29.9)	37	46.2
	Obese (≥30)	23	28.8
	Mean ± SD (kg/m²)	27.5 ± 3.9	
Menstrual irregularity	Present	58	72.5
	Absent	22	27.5
Clinical hyperandrogenism	Present	52	65
	Absent	28	35
Duration of infertility (years)		3.2 ± 1.4	
Baseline AMH (ng/mL)		8.4 ± 2.1	

Table II presents the mean serum AMH levels before and after 3 months of metformin therapy. The mean AMH significantly decreased from 8.4 ± 2.1 ng/mL at baseline to 6.1 ± 1.8 ng/mL after treatment (mean difference 2.3 ± 1.2 ng/mL, $p < 0.001$).

Table II
Pre- and Post-Treatment Serum AMH Levels (*n* = 80).

Parameter	Baseline (Mean ± SD)	After 3 Months (Mean ± SD)	Mean Difference	p-value
AMH (ng/mL)	8.4 ± 2.1	6.1 ± 1.8	2.3 ± 1.2	<0.001

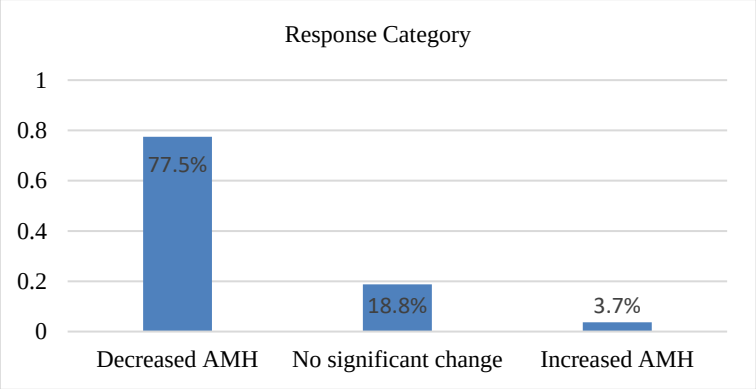

Figure I Response of Serum AMH to Metformin Therapy (*n* = 80).

Figure I illustrate the response of serum AMH to metformin therapy. Most participants (62/80, 77.5%) experienced a decrease in AMH, 15 participants (18.8%) had no significant change, and 3 participants (3.7%) showed an increase.

Table III shows the stratified analysis of AMH change according to BMI category. Obese participants exhibited the greatest reduction in AMH levels (8.7 ± 2.3 to 5.9 ± 1.7 ng/mL, p < 0.001), followed by overweight (8.3 ± 2.0 to 6.2 ± 1.9 ng/mL, p < 0.001) and normal weight participants (7.8 ± 1.9 to 6.5 ± 1.6 ng/mL, p = 0.004).

Table III
Serum AMH Change According to BMI Category (*n* = 80).

BMI Category	n	Baseline AMH (Mean ± SD)	After Treatment (Mean ± SD)	Mean Reduction	p-value
Normal weight (18.5–24.9 kg/m²)	20	7.8 ± 1.9	6.5 ± 1.6	1.3	0.004
Overweight (25–29.9 kg/m²)	37	8.3 ± 2.0	6.2 ± 1.9	2.1	<0.001
Obese (≥30 kg/m²)	23	8.7 ± 2.3	5.9 ± 1.7	2.8	<0.001

Table IV shows the correlation of baseline AMH with BMI and with the magnitude of AMH reduction. Baseline AMH was positively correlated with BMI (r = 0.41, p < 0.001) and with AMH reduction (r = 0.52, p < 0.001), indicating that participants with higher baseline AMH levels tended to have higher BMI and greater AMH reduction after metformin therapy.

Table IV
Correlation Between Baseline AMH and BMI, and AMH Reduction (*n* = 80).

Variable Pair	Correlation Coefficient (r)	p-value
Baseline AMH vs BMI	0.41	<0.001
Baseline AMH vs AMH Reduction	0.52	<0.001

DISCUSSION

Polycystic Ovary Syndrome is a common endocrine disorder and a leading cause of anovulatory infertility in women of reproductive age, characterized by hyperandrogenism, ovulatory dysfunction, and metabolic disturbances. Anti-Mullerian Hormone serves as an important marker of ovarian follicular activity and is typically elevated in women with this condition, reflecting altered folliculogenesis. The findings of the present study demonstrate that metformin therapy is associated with a significant reduction in serum AMH levels among infertile women with Polycystic Ovary Syndrome, with greater reductions observed in those with higher body mass index and baseline AMH levels. These results highlight the potential role of metformin not only in improving metabolic parameters but also in modulating ovarian hormonal dynamics, emphasizing its clinical relevance in the management of infertility related to Polycystic Ovary Syndrome.

In the present study, the baseline demographic and clinical characteristics of the 80 infertile women with PCOS indicated that the majority were aged 26–30 years (45.0%), with a mean age of 29.1 ± 4.5 years. Most participants were overweight (46.2%) or obese (28.8%), with a mean BMI of 27.5 ± 3.9 kg/m². Menstrual irregularity and clinical hyperandrogenism were observed in 72.5% and 65% of participants, respectively. These findings are consistent with previous reports, such as Kayali et al., who found that a high proportion of infertile women with PCOS were overweight or obese (74.0%) and exhibited menstrual irregularity and hyperandrogenism [11], and Sachdeva et al., who similarly reported that most infertile PCOS women were overweight or obese [12], reinforcing the well-established association between PCOS and increased adiposity. The mean duration of infertility in our cohort was 3.2 ± 1.4 years, and the baseline AMH level was 8.4 ± 2.1 ng/mL, reflecting the typical reproductive and hormonal profile

observed in infertile women with PCOS. Collectively, these results corroborate existing evidence that PCOS in infertile women is frequently associated with overweight or obesity, menstrual disturbances, and hyperandrogenism.

Metformin therapy for 3 months in this study resulted in a significant reduction in serum AMH levels, with mean AMH decreasing from 8.4 ± 2.1 ng/mL at baseline to 6.1 ± 1.8 ng/mL post-treatment (mean difference 2.3 ± 1.2 ng/mL, $p < 0.001$). These findings are consistent with Foroozanfard et al., who reported a significant decline in AMH from 10.0 ± 3.75 ng/mL to 7.8 ± 3.7 ng/mL ($p = 0.008$) after 8 weeks of metformin therapy in a cohort of 30 infertile women with PCOS [13], demonstrating the short-term efficacy of metformin in lowering AMH levels. Similarly, Zhou et al., in a systematic review and meta-analysis of 14 studies encompassing approximately 257 women with PCOS, observed an overall significant decrease in AMH following metformin treatment, with the greatest reductions occurring in younger women and those receiving therapy for ≤6 months [14]. Collectively, these results support the notion that metformin effectively reduces elevated AMH levels in infertile women with PCOS, likely reflecting its impact on follicular activity and ovarian function.

The majority of women in the present study experienced a decrease in serum AMH levels after metformin therapy, while a smaller proportion showed no significant change or an increase. These findings are consistent with Tomova et al., who reported that women with PCOS treated with metformin for 6 months exhibited significant reductions in AMH among clinical responders, whereas non-responders occasionally showed increases, reflecting the heterogeneity in ovarian response [15]. Similarly, Mehdinezhad et al., in meta-analyses of multiple clinical trials, found that most women with PCOS experienced significant decreases in AMH following metformin treatment, particularly with short-term therapy comparable to the present study [16]. These observations indicate that metformin effectively reduces elevated AMH levels in most infertile women with PCOS, while a smaller subset may exhibit stable or increased levels, likely due to individual differences in metabolic profile and ovarian responsiveness.

Metformin therapy in the current study also led to significant reductions in serum AMH across all BMI categories, with the greatest reduction observed in obese participants, followed by overweight and normal-weight groups. These findings align with Zhou et al., whose meta-analyses reported overall significant decreases in AMH after metformin treatment and highlighted that baseline metabolic and demographic factors, including BMI, can influence the magnitude of AMH reduction [14], reflecting variability across patient subgroups. Similarly, Kriseman et al. reported that BMI interacts with AMH regulation in women with PCOS, with higher BMI associated with altered AMH dynamics, suggesting that body composition may modulate ovarian response to interventions like metformin [17]. Collectively, these observations support the notion that the degree of AMH reduction following metformin therapy is influenced by BMI, with greater decreases seen in women with higher adiposity.

In this study, baseline serum AMH was positively correlated with BMI ($r = 0.41$, $p < 0.001$) and with the magnitude of AMH reduction following metformin therapy ($r = 0.52$, $p < 0.001$), indicating that women with higher baseline AMH tended to have higher BMI and experienced greater declines in AMH. These findings are consistent with Kriseman et al., who reported a significant inverse correlation between AMH and BMI in women with PCOS [17], highlighting that adiposity influences ovarian hormone levels. Similarly, Misra et al. observed that BMI modulates AMH levels across PCOS subgroups, with lean PCOS women showing stronger correlations, suggesting that body composition can affect ovarian function and hormonal markers [18]. Additionally, Foroozanfard et al. demonstrated that higher BMI was associated with larger decreases in AMH after metformin treatment [13], supporting the notion that baseline metabolic status can influence both AMH levels and the response to therapy. Collectively, these studies corroborate the present findings, emphasizing that BMI plays a significant role in determining baseline AMH and its modulation following metformin treatment in women with PCOS.

LIMITATIONS

This study had some limitations:

- It was a single-center study. A larger, multi-center study is needed to reach more definitive conclusions.
- The study's limited geographic scope may introduce sample bias, potentially affecting the broader applicability of the findings.

CONCLUSION

Polycystic Ovary Syndrome is commonly associated with elevated AMH levels and impaired ovarian function in infertile women. In this study, metformin therapy effectively reduced serum AMH levels, with most participants showing a decrease while a smaller proportion exhibited no change or an increase. The reduction in AMH was observed across all BMI categories, with greater decreases in women with higher adiposity. Baseline AMH levels were positively associated with BMI and the magnitude of AMH reduction, indicating that women with higher initial AMH and body mass tended to respond more robustly. These findings suggest that metformin has a significant modulatory effect on ovarian hormonal activity in infertile women with PCOS, and that individual characteristics such as BMI may influence treatment response.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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