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Correlation of anti-mullerian hormone (AMH) with hyperandrogenism, insulin resistance and metabolic parameters in adolescent PCOS

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Abstract

Background: Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder in adolescents, characterized by hyperandrogenism and insulin resistance. Anti-Müllerian Hormone (AMH) has been postulated as a potential biomarker in PCOS, but its correlation with metabolic and hormonal profiles in adolescents remains underexplored.

Objective: This study aimed to investigate the correlation of AMH with hyperandrogenism, insulin resistance, and metabolic parameters in adolescents diagnosed with PCOS.

Methods: A prospective cohort study was conducted involving 100 adolescent females (50 with PCOS and 50 healthy controls), aged 12-19 years, at a tertiary care center. Clinical assessments, blood tests (including AMH, testosterone, fasting glucose, and insulin levels), and ultrasound evaluations were performed. Statistical analyses included independent t-tests, Pearson's correlation, and multiple regression analysis.

Results: The PCOS group exhibited significantly higher AMH (9.2 ± 4.1 ng/mL) and testosterone levels (55 ± 18 ng/dL) compared to controls (AMH: 4.5 ± 2.3 ng/mL, Testosterone: 35 ± 12 ng/dL, $p < 0.001$). Additionally, the PCOS group showed increased insulin resistance (HOMA-IR: 3.6 ± 1.2 vs. 2.0 ± 0.8, $p < 0.001$) and altered lipid profiles (total cholesterol: 190 ± 30 mg/dL, HDL: 45 ± 8 mg/dL). Significant correlations were found between AMH levels and testosterone ($r = 0.62$, $p < 0.001$), HOMA-IR ($r = 0.47$, $p < 0.001$), and BMI ($r = 0.35$, $p = 0.01$). Multiple regression analysis identified BMI, fasting insulin, and testosterone as significant predictors of AMH levels.

Conclusion: AMH levels are significantly elevated in adolescents with PCOS and correlate with hyperandrogenism, insulin resistance, and metabolic disturbances. These findings highlight the potential

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of AMH as a biomarker in adolescent PCOS, aiding in early diagnosis and management. Further research is needed to explore the therapeutic implications of targeting AMH in PCOS treatment strategies.

Keywords: Polycystic Ovary Syndrome, Anti-Müllerian Hormone, Hyperandrogenism, Insulin Resistance, Adolescents.

Introduction

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting 5-10% of women of reproductive age and is often associated with hyperandrogenism, insulin resistance, and various metabolic disturbances [1]. The etiology of PCOS remains multifactorial, encompassing genetic, environmental, and lifestyle factors, which contribute to its heterogeneous clinical presentation [2]. A pivotal biomarker in understanding and managing PCOS is Anti-Müllerian Hormone (AMH), a glycoprotein of the transforming growth factor-β (TGF-β) family, primarily secreted by granulosa cells of ovarian follicles [3].

AMH plays a crucial role in folliculogenesis and ovarian reserve estimation [4]. However, its role extends beyond reproductive health, as emerging evidence suggests a correlation between elevated AMH levels and the various clinical manifestations of PCOS, particularly in adolescents [5]. Hyperandrogenism, a cardinal feature of PCOS, is characterized by excessive production of androgens, leading to clinical manifestations such as hirsutism, acne, and alopecia [6]. The relationship between AMH and hyperandrogenism in adolescent PCOS is complex, and the underlying mechanisms are still being elucidated [7].

Insulin resistance, another hallmark of PCOS, is intricately linked with metabolic syndrome, comprising a cluster of conditions like obesity, hypertension, dyslipidemia, and glucose intolerance [8]. In PCOS, insulin resistance exacerbates hyperandrogenism through various mechanisms, including the stimulation of ovarian androgen production and reduction of hepatic sex hormone-binding globulin (SHBG) synthesis [9]. Studies have shown that AMH levels may be indicative of the degree of insulin resistance and metabolic disturbances in PCOS, offering potential clinical insights [10].

In adolescents, PCOS poses unique challenges. The overlap of normal pubertal development with the symptoms of PCOS makes the diagnosis and management particularly complex [11]. Adolescent girls with PCOS are at a higher risk of developing long-term complications such as type 2 diabetes, cardiovascular diseases, and infertility [12]. Understanding the interplay between AMH, hyperandrogenism, and insulin resistance in this demographic is crucial for early intervention and prevention of these adverse outcomes.

The increased levels of AMH observed in PCOS patients are attributed to the increased number of small antral follicles and altered granulosa cell activity [13]. These elevated AMH levels are proposed to contribute to the anovulatory state common in PCOS by inhibiting the growth of dominant follicles and disrupting folliculogenesis [14]. Furthermore, the high AMH levels in PCOS have been linked with the severity of hyperandrogenism, suggesting a potential role of AMH in the androgen excess that characterizes this disorder [15].

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Hyperandrogenism in PCOS is primarily driven by ovarian and adrenal androgen overproduction. The precise mechanism by which AMH influences androgen levels in PCOS is not fully understood. However, it is hypothesized that AMH may exacerbate hyperandrogenism by enhancing the sensitivity of the ovaries to luteinizing hormone (LH), thus stimulating excessive androgen production [16]. The clinical implications of this relationship are significant, as hyperandrogenism is responsible for many of the dermatological and reproductive issues faced by PCOS patients [17].

Insulin resistance in PCOS is a critical factor that influences both reproductive and metabolic profiles. Elevated AMH levels have been associated with insulin resistance and related metabolic parameters like obesity and dyslipidemia in PCOS [18]. This association is particularly relevant in the adolescent population, where early metabolic disturbances can set the stage for chronic conditions in adulthood [19]. The potential of AMH as a biomarker for insulin resistance in PCOS is an area of active research, with implications for early detection and management of metabolic complications [20].

Adolescent PCOS is a unique entity, and the role of AMH in this age group is becoming increasingly recognized. Adolescents with PCOS often present with more severe symptoms compared to adults, including marked hyperandrogenism and metabolic disturbances [21]. Elevated AMH levels in adolescents with PCOS could serve as an early indicator of the disorder, aiding in timely diagnosis and intervention [22]. Moreover, tracking AMH levels over time might provide insights into the progression of PCOS and the effectiveness of therapeutic interventions [23].

In summary, AMH is emerging as a key player in the pathophysiology of PCOS, particularly in adolescents. Its correlation with hyperandrogenism, insulin resistance, and metabolic disturbances offers a window into the complex interplay of factors contributing to this disorder. Further research in this area is essential to unravel the full potential of AMH as a diagnostic and prognostic tool in PCOS, paving the way for more targeted and effective treatments.

Aims and Objectives of the Study

- **Evaluate AMH Levels in Adolescents with PCOS:** Measure and compare AMH levels in adolescents with and without PCOS.
- **Correlate AMH with Hyperandrogenism:** Explore the relationship between AMH levels and signs of hyperandrogenism in adolescent PCOS patients.
- **Assess AMH and Insulin Resistance Link:** Investigate the association between AMH levels and insulin resistance in these patients.
- **Study AMH and Metabolic Parameters:** Examine the correlation between AMH levels and metabolic parameters like BMI and lipid profiles in adolescent PCOS.
- **Determine AMH's Predictive Value in PCOS Diagnosis:** Evaluate the effectiveness of AMH as a biomarker for early PCOS diagnosis in adolescents.

Materials and Methods

Study Design and Setting

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This study was designed as a prospective cohort study, conducted over a period of one year at a tertiary care center. The study aimed to investigate the correlation of Anti-Müllerian Hormone (AMH) with hyperandrogenism, insulin resistance, and metabolic parameters in adolescents diagnosed with Polycystic Ovary Syndrome (PCOS).

Participants

The study included 100 adolescent females aged between 12 and 19 years, with 50 diagnosed with PCOS based on the Rotterdam criteria and 50 healthy controls matched for age and BMI. The inclusion criteria for the PCOS group were the presence of two out of three of the following: oligo- or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound. The exclusion criteria included other endocrine disorders, diabetes, and current use of hormonal or insulin-sensitizing medication.

Data Collection Procedure

Data were collected through clinical evaluations, blood tests, and questionnaires. Clinical assessments included measurements of height, weight, BMI, and signs of hyperandrogenism (hirsutism, acne, alopecia). Blood samples were drawn to measure AMH levels, fasting glucose and insulin, lipid profiles, and testosterone levels. Ultrasound examinations were conducted to assess ovarian morphology.

Statistical Analysis

Statistical analysis was performed using SPSS software. Descriptive statistics were used to summarize the characteristics of the study population. Comparative analysis between the PCOS group and control group was conducted using independent t-tests for continuous variables and chi-square tests for categorical variables. The correlation between AMH levels and other variables (hyperandrogenism, insulin resistance, and metabolic parameters) was assessed using Pearson's correlation coefficient. Multiple regression analysis was used to adjust for potential confounders. A p-value of less than 0.05 was considered statistically significant.

Results

Table 1: Baseline Characteristics of Participants

In terms of age, the study groups were closely matched, with the PCOS group averaging 16.3 ± 1.5 years and the control group at 16.2 ± 1.4 years. This similarity in age supports the validity of comparisons made between the groups. However, a notable difference was observed in Body Mass Index (BMI), where the PCOS group had a higher mean BMI (24.5 ± 3.2 kg/m²) compared to the control group (22.1 ± 2.8 kg/m²). This finding aligns with existing literature that suggests a higher prevalence of increased BMI in adolescents with PCOS.

Table 2: Clinical and Biochemical Features

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The clinical presentation of PCOS was evident in the comparison of hirsutism and acne presence. The PCOS group had a significantly higher mean Ferriman-Gallwey score (8.3 ± 2.1) indicative of hirsutism, compared to the control group (3.1 ± 1.5), with a p-value of <0.001. Additionally, acne was more prevalent in the PCOS group, affecting 70% of participants, compared to only 20% in the control group, further underscoring the clinical manifestations of hyperandrogenism in PCOS.

Table 3: Hormonal Profile Comparison

Hormonal differences were stark, with the PCOS group showing significantly elevated levels of AMH (9.2 ± 4.1 ng/mL) and testosterone (55 ± 18 ng/dL) compared to the control group (AMH: 4.5 ± 2.3 ng/mL, Testosterone: 35 ± 12 ng/dL), both with p-values of <0.001. These differences highlight the hormonal imbalances characteristic of PCOS, particularly the elevation in androgens.

Table 4: Insulin Resistance and Glycemic Parameters

Insulin resistance parameters were significantly different between the groups. The PCOS group exhibited higher fasting glucose (95 ± 12 mg/dL vs. 88 ± 10 mg/dL) and fasting insulin levels (15 ± 5 µIU/mL vs. 9 ± 3 µIU/mL), along with a higher mean HOMA-IR score (3.6 ± 1.2 vs. 2.0 ± 0.8), all indicating greater insulin resistance in the PCOS group.

Table 5: Metabolic Parameters

In terms of metabolic health, the PCOS group had worse profiles with a mean total cholesterol level of 190 ± 30 mg/dL compared to 170 ± 25 mg/dL in the control group, and a lower HDL level (45 ± 8 mg/dL vs. 55 ± 10 mg/dL), with p-values of 0.02 and 0.01, respectively. These findings suggest an altered lipid profile in adolescents with PCOS, which is a risk factor for cardiovascular diseases.

Table 6: Correlation of AMH Levels with Hyperandrogenism and Metabolic Parameters

The correlation analysis revealed significant relationships between AMH levels and other variables. A strong correlation was found between AMH and testosterone levels (Pearson correlation coefficient = 0.62, $p < 0.001$), suggesting a link between elevated AMH and androgen excess. Additionally, AMH showed moderate correlations with HOMA-IR (0.47) and BMI (0.35), both statistically significant, indicating its potential role in the metabolic aspects of PCOS.

Table 7: Multiple Regression Analysis for Predictors of AMH Levels

Multiple regression analysis identified BMI, fasting insulin, and testosterone as significant predictors of AMH levels, with beta coefficients of 0.45, 0.37, and 0.50, respectively. These results suggest that these factors contribute significantly to the variation in AMH levels among adolescents with PCOS, highlighting the complex interplay of metabolic and hormonal factors in this condition.

In summary, the findings from these tables underscore the hormonal, metabolic, and clinical differences between adolescents with PCOS and healthy controls, with significant correlations noted between AMH levels and various aspects of PCOS.

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Table 1: Baseline Characteristics of Participants

Variable	PCOS Group (N=50)	Control Group (N=50)
Age (years)	Mean ± SD: 16.3 ± 1.5	Mean ± SD: 16.2 ± 1.4
BMI (kg/m^2)	Mean ± SD: 24.5 ± 3.2	Mean ± SD: 22.1 ± 2.8

Table 2: Clinical and Biochemical Features of PCOS Participants vs. Controls

Feature	PCOS Group	Control Group	P-value
Hirsutism (Ferriman-Gallwey Score)	Mean ± SD: 8.3 ± 2.1	Mean ± SD: 3.1 ± 1.5	<0.001
Acne Presence	70% (35/50)	20% (10/50)	<0.001

Table 3: Hormonal Profile Comparison

Hormone	PCOS Group	Control Group	P-value
AMH (ng/mL)	Mean ± SD: 9.2 ± 4.1	Mean ± SD: 4.5 ± 2.3	<0.001
Testosterone (ng/dL)	Mean ± SD: 55 ± 18	Mean ± SD: 35 ± 12	<0.001

Table 4: Insulin Resistance and Glycemic Parameters

Parameter	PCOS Group	Control Group	P-value
Fasting Glucose (mg/dL)	Mean ± SD: 95 ± 12	Mean ± SD: 88 ± 10	0.03
Fasting Insulin (µIU/mL)	Mean ± SD: 15 ± 5	Mean ± SD: 9 ± 3	<0.001
HOMA-IR	Mean ± SD: 3.6 ± 1.2	Mean ± SD: 2.0 ± 0.8	<0.001

Table 5: Metabolic Parameters

Parameter	PCOS Group	Control Group	P-value
Total Cholesterol (mg/dL)	Mean ± SD: 190 ± 30	Mean ± SD: 170 ± 25	0.02

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HDL (mg/dL)	Mean ± SD: 45 ± 8	Mean ± SD: 55 ± 10	0.01

Table 6: Correlation of AMH Levels with Hyperandrogenism and Metabolic Parameters

Correlation	AMH vs. Testosterone	AMH vs. HOMA-IR	AMH vs. BMI
Pearson Correlation Coefficient	0.62	0.47	0.35
P-value	<0.001	<0.001	0.01

Table 7: Multiple Regression Analysis for Predictors of AMH Levels

Predictor Variable	Beta Coefficient	Standard Error	P-value
BMI	0.45	0.13	0.01
Fasting Insulin	0.37	0.15	0.02
Testosterone	0.5	0.16	<0.001

Discussion

The findings of this study illuminate several critical aspects of Polycystic Ovary Syndrome (PCOS) in adolescents, particularly focusing on the role of Anti-Müllerian Hormone (AMH) in its pathophysiology. The elevated levels of AMH in the PCOS group, as compared to controls, align with previous research underscoring the role of AMH as a biomarker in PCOS [23]. AMH, known for its role in follicular development, has been increasingly recognized for its involvement in the hormonal imbalances characteristic of PCOS, particularly hyperandrogenism [24].

The study's findings regarding hyperandrogenism, evidenced by higher testosterone levels and clinical manifestations such as hirsutism and acne in the PCOS group, corroborate with existing literature that identifies hyperandrogenism as a central feature of PCOS [25]. The significant correlation between AMH and testosterone levels in our study suggests that AMH could be contributing to or be a marker of the hyperandrogenic state in PCOS [26].

Furthermore, the observed insulin resistance in the PCOS group, as indicated by higher fasting insulin levels and HOMA-IR scores, is consistent with previous studies that have established insulin resistance as a key component of PCOS, contributing to its metabolic complications [27]. The correlation of AMH with

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insulin resistance metrics in our study provides new insights into the potential role of AMH in the metabolic disturbances associated with PCOS [28].

The altered lipid profiles in the PCOS group, particularly the higher total cholesterol and lower HDL levels, point towards an increased risk of cardiovascular diseases, which has been a concern in PCOS populations [29]. These metabolic abnormalities in PCOS adolescents underscore the importance of early diagnosis and intervention to mitigate long-term risks.

The multiple regression analysis revealing BMI, fasting insulin, and testosterone as significant predictors of AMH levels suggests a multifactorial influence on AMH levels in PCOS, involving both metabolic and hormonal factors [30]. This finding highlights the complex interplay of different physiological systems in PCOS and reinforces the importance of a comprehensive approach to its management.

Conclusion

This study reinforces the role of AMH as a significant biomarker in adolescent PCOS, correlating strongly with hyperandrogenism and insulin resistance. The findings emphasize the multifaceted nature of PCOS, involving interrelated metabolic and hormonal disturbances. Early recognition and management of these factors are crucial in addressing the long-term health risks associated with PCOS. Future research should focus on exploring the therapeutic implications of these findings, particularly the potential of targeting AMH pathways, to improve outcomes in adolescents with PCOS.

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