Effects of Hypoxic Environment on Ovulatory Dysfunction and Hyperandrogenemia in High-Altitude Residents with Polycystic Ovary Syndrome

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Abstract: Objective: To investigate the effects of hypoxic environment on ovulatory dysfunction and hyperandrogenemia in patients with polycystic ovary syndrome living at high altitude, and to provide a theoretical basis for the clinical treatment of polycystic ovary syndrome in high-altitude areas. Methods: A total of 86 patients with polycystic ovary syndrome admitted to our hospital from January 2025 to January 2026 were selected as research subjects and divided into a control group and an observation group according to residential environment, with 43 cases in each group. The control group consisted of patients living in plain areas, and the observation group consisted of patients living in a high-altitude hypoxic environment. Indicators related to ovulatory function, hyperandrogenemia and hypoxia were compared between the two groups, and statistical methods were used to analyze the differences between the two groups of data. Results: The ovulation rate (23.26%) in the observation group was significantly lower than that in the control group (48.84%), and the incidence of oligomenorrhea (58.14%) and amenorrhea (25.58%) was significantly higher than that in the control group (27.91%, 6.98%), with statistically significant differences. The levels of testosterone (3.12±0.68 nmol/L) and androstenedione (9.76±1.58 nmol/L) in the observation group were significantly higher than those in the control group (2.35±0.52 nmol/L, 7.82±1.35 nmol/L), while the estradiol level (125.38±22.19 pmol/L) was significantly lower than that in the control group (158.63±25.47 pmol/L), with statistically significant differences. The blood oxygen saturation (88.35±2.16%) in the observation group was significantly lower than that in the control group (96.52±1.23%), and the red blood cell count (5.67±0.58×10^{12}/L) was significantly higher than that in the control group (4.58±0.42×10^{12}/L), with statistically significant differences. Conclusion: Chronic hypoxia in plateau regions exacerbates ovulatory dysfunction and hyperandrogenism in patients with PCOS. Clinical management strategies should be tailored to hypoxic conditions to improve physiological outcomes in this population.

Keywords: Hypoxic environment; High altitude; Polycystic ovary syndrome; Ovulatory dysfunction; Hyperandrogenemia

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Introduction

Polycystic ovary syndrome (PCOS), also known as Stein-Leventhal syndrome, is a common endocrine and metabolic disorder among women of reproductive age. Its core manifestations include abnormal ovulatory function, hyperprolactinemia, and polycystic changes in the ovaries, often accompanied by menstrual disorders, infertility, hirsutism, acne and other uncomfortable symptoms, which significantly affect patients' physical and mental health as well as quality of life [1]. The global prevalence of PCOS ranges from 6% to 20%. However, in plateau areas, the significant decrease in atmospheric oxygen partial pressure creates a unique hypoxic environment that profoundly impacts the human endocrine system [2]. Chronic exposure to a high-altitude hypoxic environment activates the sympathetic nervous system and hypoxia-inducible factors, which interfere with the function of the hypothalamic-pituitary-ovarian (HPO) axis, thereby inhibiting follicular development and ovulation. Furthermore, it exacerbates insulin resistance and promotes fat accumulation, thus inducing or aggravating hyperandrogenemia [3-5]. At present, studies on the effects of a hypoxic environment on high-altitude residents with PCOS are limited, and recent data from 2025–2026 for high-altitude patients are lacking [6]. Therefore, this study enrolled 86 PCOS patients to compare ovulatory function and hormone levels between patients living in plains and those living in high-altitude

hypoxic environments, explore the mechanisms of hypoxic effects, and provide a clinical reference for the precise diagnosis and treatment of PCOS in high-altitude regions.

1.Materials and Methods

1.1 Study Subjects

A total of 86 PCOS patients who visited our hospital and affiliated hospitals from January 2025 to January 2026 were enrolled. Inclusion criteria: diagnosis of PCOS based on at least one of the following: ovulatory dysfunction, hyperandrogenemia, or polycystic ovarian morphology. Exclusion criteria: other endocrine diseases, organic ovarian lesions, severe hepatic and renal insufficiency, recent use of hormonal drugs and contraceptives. All patients voluntarily participated in this study and signed informed consent forms. Patients were divided into a control group and an observation group according to their living environment, with 43 cases in each group. The control group consisted of patients who had long-term residence in plain areas (altitude < 500 m) with no history of high-altitude residence. The observation group consisted of patients who had long-term residence in high-altitude areas (altitude > 3000 m) for at least one year, living under chronic hypoxic conditions. No statistically significant differences were found between the two groups in general characteristics such as age, disease duration, and body mass index, indicating comparability.

1.2 Methods

1.2.1 Control Group

Patients in the control group were all in a plain environment with an altitude below 500 meters and received routine examinations and basic treatment according to conventional protocols. Routine examinations included gynecological examination, transvaginal ultrasound, and fasting venous blood test. Transvaginal ultrasound was performed on days 3 to 5 of the menstrual cycle to screen for polycystic ovarian morphology and organic uterine lesions. Fasting venous blood samples were collected after 8 to 12 hours of overnight fasting. Fasting venous blood samples were collected after an overnight fast of 8–12 hours to measure hormone levels, fasting glucose, and insulin levels, excluding insulin resistance and other endocrine abnormalities .Basic interventions included dietary guidance with a low glycemic index and high dietary fiber diet pattern, controlling total daily calorie intake, reducing high-sugar, high-fat and high-salt foods, with carbohydrates accounting for 50% to 60% of total calories, protein 15% to 20%, and fat 20% to 30%. Exercise intervention adopted moderate-intensity aerobic exercise 3 to 5 times a week, 30 to 40 minutes each time, including brisk walking, jogging, swimming, etc. Exercise intensity was controlled at (220 − age) × 60% to 70%. No hormonal drugs or contraceptives were used during the whole period. Ovulation was monitored by transvaginal ultrasound starting from day 10 of the menstrual cycle, once a day until follicle rupture or anovulation was confirmed, for 3 consecutive menstrual cycles. Hormone levels were reexamined by collecting fasting venous blood 3 to 5 days after the end of each menstrual cycle.

1.2.2 Observation Group

Patients in the observation group had long-term residence in plateau areas (> 3000 m) for more than one year and received the same routine examinations and basic interventions as the control group, with the same examination items, examination time, diet and exercise intervention standards. No hormonal drugs or contraceptives were used during the whole study period. On the basis of the control group, monitoring of hypoxia-related indicators was added. The monitoring methods and frequency of ovulation and hormone levels were the same as those in the control group. Hypoxia-related indicators were monitored by finger pulse oximeter and automatic blood cell analyzer. Blood oxygen saturation (SpO_2)was measured once every early morning in a resting state (10 minutes of bed rest). Fasting venous blood was collected once every two weeks to detect red blood cell count. At the same time, daily hypoxia-related discomforts such as dizziness, fatigue, chest distress and shortness of breath were recorded, including the occurrence time, duration and remission of symptoms, which were summarized and included in

statistical analysis.

1.3 Outcome measures

1.3.1 Ovulatory Function Indicators

Ovulation rate and menstrual abnormalities (oligomenorrhea, amenorrhea) were recorded in both groups. Ovulation rate was monitored by transvaginal B-ultrasound once daily starting from day 10 of the menstrual cycle to observe follicular development. Ovulation was defined as follicular diameter ≥ 18 mm with follicular rupture. Monitoring was conducted for 3 consecutive menstrual cycles. The number of ovulatory cases in each cycle was counted, and the ovulation rate was calculated as (number of ovulatory cases / total number of cases × 100%). Oligomenorrhea was defined as menstrual cycle > 35 days, and amenorrhea was defined as no menstrual flow for more than 6 consecutive months. The number of cases and incidence rates of oligomenorrhea and amenorrhea were counted in both groups.

1.3.2 Hyperandrogenemia Indicators

A 5 mL fasting venous blood sample was collected from each patient in both groups after 8–12 hours of fasting. The samples were immediately sent to the laboratory and centrifuged at 3000 r/min for 10 minutes. The separated serum was stored in a -20℃ refrigerator until analysis. Serum levels of testosterone, androstenedione, and estradiol were measured by chemiluminescence assay using a fully automatic chemiluminescent immunoassay analyzer with corresponding special detection kits. Detection parameters were set strictly in accordance with the kit instructions. Standards and quality control products were included in each batch to ensure accurate and reliable results, which were then recorded.

1.3.3 Hypoxia-Related Indicators

Blood oxygen saturation at rest was measured in both groups using a finger pulse oximeter. Before measurement, patients were instructed to lie supine and rest for 10 minutes with stable breathing. The pulse oximeter was clipped to the tip of the index finger, and readings were recorded after the values stabilized. Each measurement was repeated three times, and the average value was taken as the final result. Red blood cell count was detected using an automatic blood cell analyzer. A 2 mL fasting venous blood sample was collected, placed into an anticoagulant tube, gently mixed, and sent to the laboratory for testing in strict accordance with the instrument operating procedures. The specific measured values were recorded.

1.4 Statistical Methods

SPSS 26.0 statistical software was used for data analysis. Measurement data were expressed as mean ± standard deviation, and comparison between groups was performed using t-test. Enumeration data were expressed as number of cases and percentage, and comparison between groups was performed using χ^2 test. $P < 0.05$ was considered statistically significant.

2.Results

2.1 Comparison of Ovulatory Function Indicators Between the Two Groups

The ovulation rate in the observation group was significantly lower than that in the control group, and the incidence rates of oligomenorrhea and amenorrhea were significantly higher than those in the control group, with statistically significant differences between the two groups. The detailed data are shown in Table 1.

Table 1 Comparison of ovulatory function indicators between the two groups

Group	Number of Cases	Ovulation Rate (%)	Oligomenorrhea (n, %)	Amenorrhea (n, %)
Control Group	43	48.84	12 (27.91)	3 (6.98)
Observation Group	43	23.26	25 (58.14)	11 (25.58)
χ^2/t value	–	7.352	8.217	5.443
P value	–	0.007	0.004	0.020

2.2 Comparison of Hyperandrogenemia-Related Indicators Between the Two Groups

The levels of testosterone and androstenedione in the observation group were significantly higher than those in the control group, while the estradiol level was significantly lower than that in the control group, with statistically significant differences between the two groups. The detailed data are shown in Table 2.

Table 2 Comparison of Hyperandrogenemia-Related Indicators Between the Two Groups

Group	N	Testosterone (nmol/L)	Androstenedione (nmol/L)	Estradiol (pmol/L)
Control group	43	2.35 ± 0.52	7.82 ± 1.35	158.63 ± 25.47
Observation group	43	3.12 ± 0.68	9.76 ± 1.58	125.38 ± 22.19
t value	—	5.784	5.932	6.015
P value	—	< 0.001	< 0.001	< 0.001

2.3 Comparison of Hypoxia-Related Indicators Between the Two Groups

The blood oxygen saturation in the observation group was significantly lower than that in the control group, while the red blood cell count was significantly higher than that in the control group, with statistically significant differences between the two groups. The detailed data are shown in Table 3.

Table 3 Comparison of hypoxia-related indicators between the two groups

Group	N	Blood oxygen saturation (%)	Red blood cell count ($\times 10^{12}$/L)
Control group	43	96.52 ± 1.23	4.58 ± 0.42
Observation group	43	88.35 ± 2.16	5.67 ± 0.58
t value	—	20.365	9.274
P value	—	< 0.001	< 0.001

3.Discussion

3.1 Effects of Hypoxic Environment on Ovulatory Dysfunction in High-Altitude Residents with PCOS

Ovulatory dysfunction is one of the main symptoms of polycystic ovary syndrome (PCOS), which is caused by functional disorders among the hypothalamus, pituitary gland and ovaries, or abnormal follicular development. As shown in the above results, the ovulation rate in the observation group was significantly lower than that in the control group, and the incidence rates of oligomenorrhea and amenorrhea were also significantly higher than those in the control group, indicating that the high-altitude hypoxic environment aggravates ovulatory dysfunction in patients with PCOS. In the high-altitude hypoxic environment, the partial pressure of atmospheric oxygen decreases, and long-term chronic hypoxia activates hypoxia-inducible factors, which in turn affects the function of the hypothalamic-pituitary-ovarian axis, inhibits the pulsatile secretion of gonadotropin-releasing hormone, and leads to an imbalance in the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) [7]. Insufficient secretion of FSH affects the normal development and maturation of follicles, resulting in blocked follicular development and failure to ovulate normally. The imbalance between LH and FSH further exacerbates abnormal follicular development, causing symptoms such as oligomenorrhea and amenorrhea. In addition, the sympathetic nervous system becomes excited under hypoxic conditions, increasing the secretion of epinephrine and cortisol, which further triggers ovulatory dysfunction and forms a vicious cycle [8].

3.2 Effects of Hypoxic Environment on Hyperandrogenemia in High-Altitude Residents with PCOS

Hyperandrogenemia is another major manifestation of polycystic ovary syndrome (PCOS), which mainly refers to elevated levels of androgens such as testosterone and androstenedione, leading to acne, hirsutism and other manifestations, thus aggravating endocrine disorders in patients. The results showed that the levels of testosterone and androstenedione in the observation group were higher than those in the control group, while the estradiol level was lower than that in the control group, indicating that hypoxic environment can induce or aggravate

hyperandrogenemia in patients with PCOS.

The possible mechanism is that hypoxic environment aggravates insulin resistance, which is the main cause of hyperandrogenemia in PCOS patients. Insulin resistance leads to elevated insulin levels, which in turn promotes excessive androgen secretion by ovarian stromal cells and adrenal cortex, and inhibits the metabolic inactivation of androgens in the liver, resulting in increased blood androgen levels. In addition, activation of hypoxia-inducible factors promotes the production and secretion of more androgens in the ovaries, inhibits estrogen synthesis, reduces estradiol levels, further exacerbates endocrine disorders and aggravates the symptoms of hyperandrogenemia. The unique dietary and living habits in plateau areas may indirectly cause a decrease in hormone levels, while the hypoxic environment increases hormone levels, thereby aggravating hyperandrogenemia.

3.3 Clinical Implications

Patients with polycystic ovary syndrome (PCOS) in plateau areas present more severe ovulatory dysfunction and hyperandrogenemia. Therefore, individualized intervention plans should be formulated for clinical treatment based on the characteristics of the high-altitude hypoxic environment.

First, health education for high-altitude PCOS patients should be strengthened, emphasizing scientific diet, moderate exercise, weight control, improvement of insulin resistance, and mitigation of hypoxia's impact on the endocrine system. Second, for patients with severe ovulatory dysfunction, ovulation-inducing medications may be used under medical guidance, with careful monitoring of follicular development to avoid adverse reactions. For patients with hyperandrogenemia, appropriate medications may be used to lower androgen levels, regulate menstrual cycles, and improve clinical symptoms. Additionally, attention should be paid to patients' hypoxic adaptation; oxygen therapy may be provided when necessary to alleviate hypoxic damage.

Due to the uneven distribution of medical resources in plateau areas, delayed medical treatment and missed diagnoses are common. Therefore, it is necessary to improve the level of gynecological endocrinology diagnosis and treatment in these regions, enhance early detection and treatment outcomes, and improve patients' prognosis. This study has a small sample size and is a single-center study. Future multi-center studies with larger sample sizes are needed to further explore the mechanism of hypoxic environment on PCOS patients living at high altitude, providing more reliable evidence for clinical treatment.

4.Conclusions

The high-altitude hypoxic environment aggravates ovulatory dysfunction in patients with polycystic ovary syndrome (PCOS), manifested by a decreased ovulation rate and increased incidence of oligomenorrhea and amenorrhea. It also induces or exacerbates hyperandrogenemia, characterized by elevated testosterone and androstenedione levels and reduced estradiol levels. The hypoxic environment interferes with the function of the hypothalamic-pituitary-ovarian axis and aggravates insulin resistance, thereby worsening the patient's condition. During clinical diagnosis and treatment, changes in ovulatory function and hormone levels of patients under the high-altitude hypoxic environment should be taken into account. Corresponding intervention measures should be adopted to improve ovulatory function and hormone levels, enhance clinical treatment efficacy, and improve patients' quality of life.

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