

Article

Correlation of Ultrasound Indicators with Biochemical Markers in Hyperandrogenism Syndrome

Bobokulova Sarvara Bakhtiyorovna*¹

1. Bukhara State Medical Institute named after Abu Ali ibn Sino, Bukhara, Uzbekistan

* Correspondence: boboqulova.sarvara@bsmi.uz

Abstract: According to the ultrasound results, 86% of women in the control group without reproductive disorders had a normal ovulatory cycle, while only 17.5% of women in the main group had an ovulatory cycle. The remaining 82.5% of women in the main group were found to have an anovulatory cycle. According to the results of the relationship between ultrasound parameters and hormone levels, the increase in the LH/FSH ratio was 1.8 and 1.78 times higher in women without follicular persistence and undetected dominant follicle, respectively, compared to the control group. Similar statistically significant differences were also observed in the levels of total testosterone, free testosterone, prolactin, and 25 (OH) D.

Keywords: Infertility, Hyperandrogenism, Menstrual Cycle Disorder, Anovulatory Cycle

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1. Introduction

Among endocrinopathies, hyperandrogenism occupies a leading position, contributing to ovulation disorders, recurrent pregnancy loss, or infertility. The proportion of infertility caused by hyperandrogenism exceeds 40%, while the risk of reproductive losses in cases where pregnancy occurs reaches 73% [1], [2], [3]. Menstrual function disorders, ranging from irregular periods to amenorrhea, occurring against a background of chronic anovulation, are characteristic of hyperandrogenism. These are typically accompanied by hirsutism, metabolic disturbances, pregnancy loss, and infertility [4], [5], [6].

Excessive production of androgens in the adrenal glands and/or ovaries is one of the most common causes of reproductive dysfunction. In addition, sources of hyperandrogenism include extraovarian factors: adipose tissue, insulin resistance and, as a consequence, hyperinsulinemia, which are associated with metabolic syndrome [7], [8], [9].

The restoration of reproductive function in patients with various forms of hyperandrogenism is a pressing medical and social issue. A priority direction for further research is the search for the most sensitive laboratory methods to diagnose various hyperandrogenic conditions. The identification of clinical, ultrasonographic, and endocrine-metabolic characteristics in patients with hyperandrogenism will enable the differentiation of various clinical and pathogenetic forms of this condition, allowing for effective targeted therapy aimed at restoring reproductive health [10], [11], [12].

Late complications of hyperandrogenism lead to an increased risk of developing endometrial cancer due to heightened proliferative activity. Furthermore, it creates conditions conducive to the onset of type II diabetes and cardiovascular diseases [13], [14], [15].

The high medical and social significance of syndromes associated with androgen overproduction, coupled with the limited literature data on the study of hyperandrogenism syndrome during the formation of the reproductive system, demonstrates the relevance of this research topic. Expanding the understanding of the mechanisms underlying the syndrome's development and improving diagnostic results are crucial for minimizing reproductive disorders in subsequent life periods

Purpose of research. Evaluation of the role of ultrasound indicators and biochemical markers in refining diagnostic criteria for hyperandrogenism syndrome.

2. Materials and Methods

126 women of reproductive age with signs of hyperandrogenism, who sought treatment at the reproductive center department of the Bukhara regional branch of the Republican Specialized Scientific and Practical Center for Mother and Child, were included in the study. Additionally, 32 healthy women of the same age without reproductive disorders were taken as a control group. Anamnestic-clinical examination, anthropometry, ultrasound, folliculometry, and laboratory studies were conducted. Blood levels of FSH, LH, prolactin, total testosterone, DHEA-S, 17-OH-progesterone, TSH, free T4, and 25 (OH) D were measured using the CLIA method with a "Maglumi 800" analyzer manufactured by Shanghai International Holding for Snibe Diagnostic. Hormones were assessed on days 2-5 of the menstrual cycle. Laboratory analyses were performed at the "Standard Diagnostics" laboratory. Reference ranges provided for the CLIA method were used to compare the obtained results.

3. Results and Discussion

Four ultrasound markers were examined in the main group of women with hyperandrogenism ($n=126$) and in the group of women without reproductive function disorders ($n=32$). Specifically, the study focused on changes in uterine size, M-Echo indicators corresponding to the menstrual cycle, ovarian size, and follicular reserve markers. The correlation between these markers and the state of hyperandrogenism (GA) was established. According to the results, the number of patients with normal uterine size in the main group was 112 (89%), while in the control group it was 31 (97%). On the other hand, hypoplasia was detected in 14 (11%) patients in the main group, whereas in the control group it was found in only 1 (3%) subject ($p>0.05$; $\chi^2 = 1.89$). Based on these findings, it was concluded that there is no statistically significant association between the ultrasound marker of uterine size and HA in women with HA (Figure 1, A).

Furthermore, the correspondence of M-Echo status to the menstrual cycle was observed in 30 (94%) patients in the control group and 65 (52%) patients in the main group. In 61 (48%) women in the main group, the M-Echo status did not correspond to the day of menstruation ($p<0.001$; $\chi^2 = 18.9$). This indicates that the mismatch of M-Echo indicators with the menstrual day is a reliable marker in patients with HA (Figure 1, C).

In addition, according to the results of ultrasound examination of ovarian dimensions, all women in the control group ($n=32$; 100%) showed normal ovarian size. In the main group, 66 patients had normal ovarian dimensions, 3 (2%) had hypoplasia, and 57 (45%) had an ovarian volume greater than 10 cm³ ($p<0.001$; $\chi^2 = 24.57$). This indicates a significant correlation between the state of HA and changes in ovarian size (Fig. 1, C).

Finally, when analyzing the results of antral follicle count or ovarian reserve in the main and control groups, the number of patients with a normal antral follicle count was 100 (79%) in the main group and 32 (100%) in the control group. Conversely, the number

of patients with a decreased follicular reserve was 26 (21%) in the main group ($p < 0.01$; $\chi^2 = 7.9$). Thus, a statistically significant relationship between the decrease in follicular reserve and GA was established (Figure 1, D).

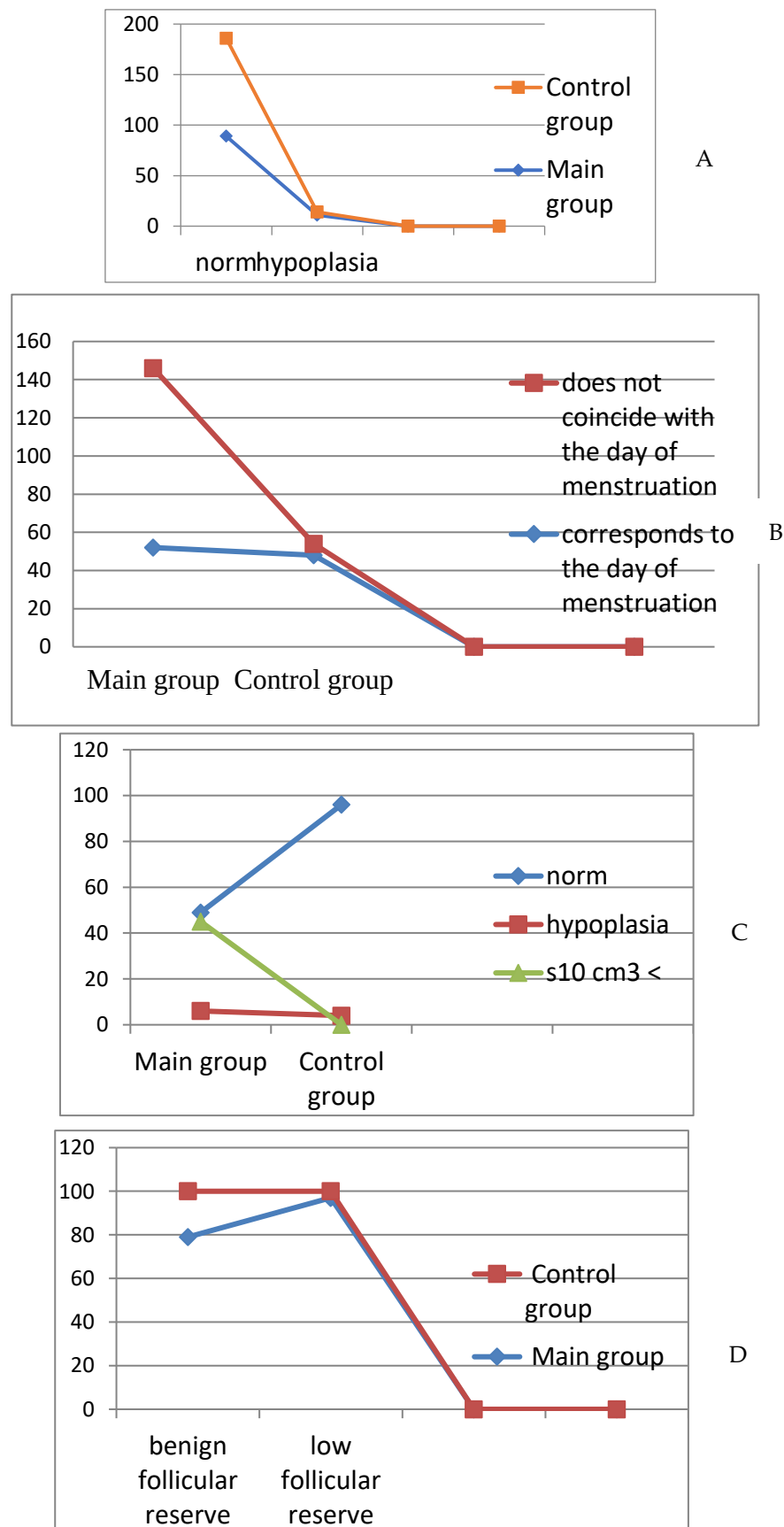


Figure 1. Results of ultrasound examination analysis for the main and control groups.

According to the results of folliculometry examination in the women participating in the study, 86% of the control group representatives were found to have an ovulatory cycle. In the main group, the number of patients with ovulatory cycles was 22 (17.50%) ($p<0.05$). Among the remaining patients, ovarian follicle persistence was detected in 69% ($n=87$) (compared to 14.4% ($n=5$) in the control group) ($p<0.05$), while in the remaining 13.50% ($n=17$), no dominant follicle was detected (no women without dominant follicles were found in the control group - ($p<0.05$)).

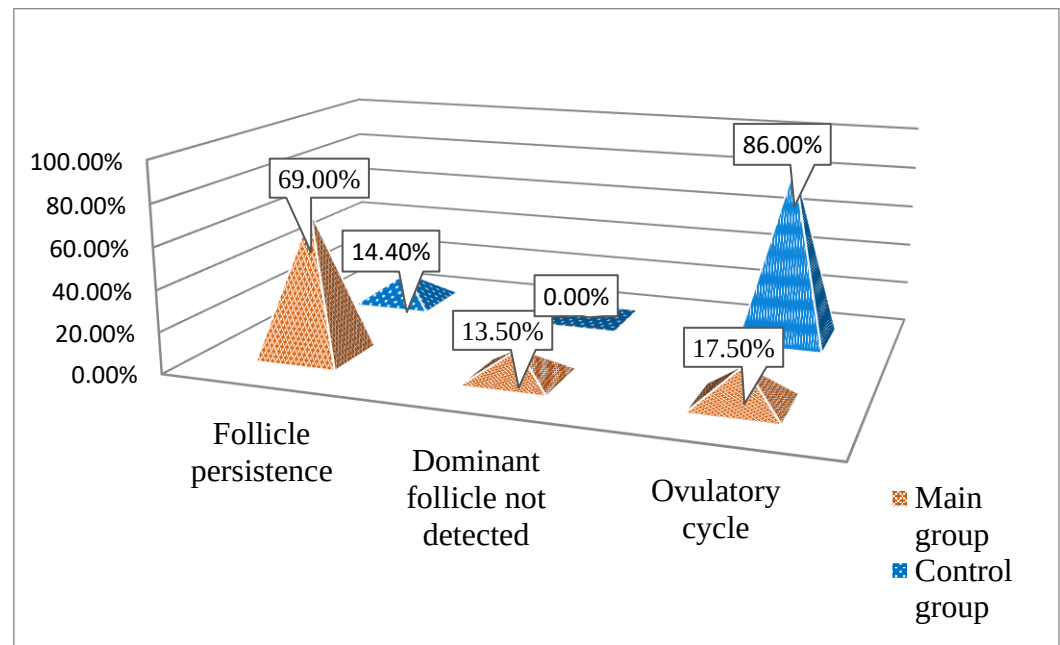


Figure 2. Results of folliculometry in patients of the main and control groups.

Furthermore, to understand the developmental mechanism of the ultrasound signs we observed, we studied the biochemical examination results of all patients by dividing them into groups based on ultrasound findings (Table 1).

As shown in Table 1, the FSH indicator results revealed a 15% decrease ($p>0.05$) in patients with follicular persistence compared to the control group, and a 10% decrease ($p>0.05$) in patients without a dominant follicle. However, in patients with an ovulatory cycle, the FSH level was found to have increased by 34% ($p<0.05$). On the other hand, statistically significant differences in LH levels were observed in all groups compared to the control group ($p<0.05$).

Table 1. The interrelation between biochemical parameters observed in patients of the main group and ultrasound signs.

Indicators	Follicle persistence	Absence of a dominant follicle	Ovulatory cycle	Control group
Follicle-stimulating hormone (FSH) (mE/ml)	6,2±0,4	6,6±0,71	9,8±0,93 ^{abc}	7,3±0,65
Luteinizing hormone (LH) (mE/ml)	11,97±0,89 ^a	12,82±0,74 ^a	12,75±1,64 ^a	7,675±0,68
LH/FSH	2,4±0,18 ^a	2,36±0,39 ^a	1,59±0,25 ^{bc}	1,34±0,12
Total testosterone (nmol/l)	3,84±0,35 ^a	3,99±0,89 ^a	4,37±0,60 ^a	1,1±0,078

Free testosterone (pg/ml)	2,76±0,115 ^a	2,72±0,13 ^a	2,42±0,11 ^{abc}	1,87±0,36
Dehydroepiandrosterone sulfate (DHEAS) (mg/dl)	386,9±18,4 ^a	322±38,0 ^a	359,3±25,8 ^a	220,4±16,36
17-OH progesterone (nmol/l)	5,53±0,39 ^a	4,00±0,74 ^{ab}	4,41±0,70 ^a	2,74±0,38
Thyrotropic hormone (TTH) (mE/ml)	2,51±0,16	2,4±0,33	2,78±0,64	2,49±0,23
Thyroxine (ng \ ml)	11,34±0,38	10,43±0,63	12,3±0,64	12,1±0,55
Prolactin (mE/ml)	310±14,2 ^a	249,2±22,8 ^b	247,2±22 ^b	254,5±10,6
25- (OH) D (ng/ml)	21,32±1,04 ^a	21,2±1,22 ^a	24,6±1,18 ^{abc}	33,24±1,78

Note: a - compared to the control group - $p < 0.05$; b - compared to the overall result of patients with follicular persistence - $p < 0.05$; c - compared to the overall result of patients without a dominant follicle - $p < 0.05$.

The LH/FSH ratio indicator showed no statistically significant difference in patients with observed ovulatory cycles compared to the control group (1.18 times higher than the control group, $p > 0.05$). However, this difference persisted in patients without follicular persistence and DF (1.8 and 1.75 times higher than the control group, respectively, $p < 0.05$ for both).

It was also found that the total testosterone levels were 3.5 ($p < 0.05$), 3.6 ($p < 0.05$), and almost 4 ($p < 0.05$) times higher in patients without follicular persistence and DF and with ovulatory cycles, respectively, compared to the control group. However, when comparing the total testosterone levels among patients with different ultrasound results, no statistically significant difference was observed. On the other hand, regarding the level of free testosterone, not only was it statistically significantly higher in all patients compared to the control group, but it was also found to be 13.5% ($p < 0.05$) and 11% ($p < 0.05$) lower in patients with ovulatory cycles compared to patients with follicular persistence and those without dominant follicles, respectively. This suggests that in patients with ovulatory cycles, although the total testosterone level is high, the relatively lower level of free testosterone (and consequently the relatively weaker pathological effect of hyperandrogenemia on women's ovaries) may have created conditions for the continuation of the ovulation process. Conversely, it is the level of free testosterone that, due to the high biological effect of androgens, may induce follicular persistence, and as a result of the chronic nature of this condition, potentially lead to its atresia.

Furthermore, DGEAS and 17-OH progesterone levels remained statistically significant compared to the control group in all types of patients with various ultrasound findings ($p < 0.05$). However, when comparing these groups with each other, no statistically significant difference was found (except for the result where patients with follicular persistence showed a 1.38 times higher 17-OH progesterone level ($p < 0.05$) compared to patients without dominant follicles). Similarly, no statistically significant difference ($p > 0.05$) was observed in TSH and T4 hormone levels among all groups based on ultrasound results.

On the other hand, regarding prolactin levels, patients with follicular persistence showed a 1.22 ($p < 0.05$) times higher result compared to the control group, and 1.25 ($p < 0.05$) times higher result compared to patients without dominant follicles and those with ovulatory cycles. Furthermore, a statistically significant difference in 25- (OH) D levels remained in all groups categorized according to ultrasound results when compared to the control group. In patients with ovulatory cycles, the level was found to be almost 16%

($p < 0.05$) higher than in groups of patients with follicular persistence and those without dominant follicles.

4. Conclusion

According to the ultrasound results, the marker indicating inconsistency of M-Echo parameters with the day of the menstrual cycle was detected at a statistically significantly higher frequency in patients with hyperandrogenism ($p < 0.001$; $\chi^2 = 18.9$). A statistically significant association was also found between decreased follicular reserve and ovarian volume greater than 10 cm³ in relation to hyperandrogenism ($p < 0.05$; $\chi^2 > 3.84$). On the other hand, in women with hyperandrogenism, no statistically significant correlation was found between the ultrasound marker of uterine size and hyperandrogenism ($p > 0.05$; $\chi^2 = 1.89$). According to the results of the correlation between ultrasound indicators and hormone levels, the increase in the LH/FSH ratio was 1.8 and 1.78 times higher in women with follicular persistence and those without a dominant follicle, respectively, compared to the control group. Similar statistically significant differences were also observed in the levels of total testosterone, free testosterone, prolactin, and 25 (OH) D.

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