

## POLYCYSTIC OVARY SYNDROME IN DUHOK: CLINICAL AND BIOCHEMICAL CHARACTERIZATION

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### ABSTRACT

**Background:** Polycystic ovary syndrome is a complex, heterogeneous disorder that affects 5-10 % of women in their reproductive age, causing a range of reproductive, metabolic, and endocrine defects characterized by chronic anovulation, hyperandrogenism, and polycystic ovaries. It manifests differently depending on many interacting factors, including environmental exposures, genetics, and lifestyle.

**Objectives:** This study aimed to assess the clinical and biochemical findings of local cases of the syndrome.

**Methods:** This cross-sectional study was carried out during the period from 01 June to 01 December 2019, at Duhok Azadi teaching hospital and the outpatient departments of Zakho maternity hospital and Kurdistan medical complex. The 108 eligible patients according to Rotterdam ESHRE/ASRM criteria were interviewed and examined by the investigator to find out and document the required data following the adopted questionnaire, which included patient's history, clinical examination, laboratory investigation, and abdominal ultrasound. The statistical package SPSS version 19 was used to analyze study variables. The statistical analyses used were *Chi-square*, Mann-Whitney test, and Unpaired *t*-test.

**Results:** The mean age of the enrolled women was  $24.3 \pm 5.54$ , the majority (81.5%) was below 30 years old and (70.6%) were overweight, (50.9%) were unmarried, and (68.5%) were having secondary school/college educational levels with (51.9%) giving the family history of PCOS. Menstrual cycle disturbances were detected in (97.2%) and infertility history (27.8%). The most common finding was hirsutism (86.1%), followed by generalized alopecia (62%). Polycystic ovaries were detected in (75.3%) on U/S examination.

**Conclusions:** In local practice, menstrual abnormalities, mostly as hypomenorrhea and oligomenorrhea, constituted the most common presentation. On the other hand, the concurrent presence of hyperandrogenism and positive ultrasound findings were more stable features and may be suggested as a better indicator for establishing the diagnosis of the syndrome locally.

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**Keywords:** Hirsutism, Hyperandrogenism, Menstrual cycle disturbances, Polycystic ovary syndrome.

The polycystic ovary syndrome (PCOS) is the most common endocrinopathy in women who are at reproductive age, and it is associated with ovarian dysfunction and metabolic disorders<sup>1</sup>. PCOS is a multifactorial

disorder, but the exact mechanisms for its development are still not clear. It is the major cause of anovulatory infertility and increases the risk of insulin resistance, obesity, cardiovascular disease, and psychosocial disorders<sup>2,3</sup>.

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The 2003 Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group concluded that no single diagnostic criterion was sufficient for a clinical diagnosis of PCOS. Two out of three criteria have to be met to fit the definition: chronic anovulation or infrequent menstrual cycles, clinical and/or biochemical hyperandrogenism, and polycystic ovaries<sup>4</sup>. Although many women in Duhok city frequently report to the local consultation clinics complaining of some of these features, the researcher couldn't find any study that investigated the syndrome. This study was designed to define the clinical and biochemical characteristics of local cases of PCOS.

## PATIENTS AND METHODS

This cross-sectional study was carried out during the period from 01 June to 01 December 2019, at Duhok Azadi teaching hospital in addition to the outpatient departments of Zakho maternity hospital and Kurdistan medical complex. The study included 108 patients who satisfied Rotterdam ESHRE/ASRM criteria. Exclusion criteria included hyper or hypothyroidism, hyperprolactinemia, Cushing syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors. After a thorough explanation of the study objectives and requirements, informed consent was taken from each eligible patient. All women were directly interviewed by the investigator in accordance with the study questionnaire using the participant's language. The study questionnaire included demographics, obstetrical and medical history. This was followed by a meticulous clinical

examination for hirsutism, acne, alopecia, and acanthosis nigricans. The weight of each participant was measured by an electronic scale (QF-2003A) bare footed ordinary wearing clothes, a wall-mounted measuring stadiometer measured the height to the nearest centimeter, converted into meters then squared and recorded, then the participant was sent to the laboratory of the hospital for determination of the required hormones (Testosterone hormone, Prolactin hormone, Thyroid-stimulating hormone (TSH), *Leutilizing* hormone and Follicular stimulation hormone as LH/FSH) using immunofluorescence assay by VIDAS technology. An abdominal U/S examination appointment was taken for each participant at the radiology department of each hospital. Competent radiologist/gynecologist did the U/S examination in each center, and the reports were written in accordance with the frame proposed in the study questionnaire. The polycystic ovary was defined as the presence of 12 or more follicles measuring 2-9mm in diameter in each ovary and/or ovarian volume > 10ml. The statistical package SPSS version 19 was used to analyze study variables. The statistical analyses used were *Chi-square*, Mann-Whitney test, and Unpaired t-test.

## RESULTS

The mean age of the enrolled women was  $24.3 \pm 5.54$ , with a range of 15-39. The majority (81.5%) were below 30 years old. The most common causes of PCOS (35.2%) were 20-24 years old. As to their educational level (42.6%) were having secondary school education. Regarding the marital status (50.9%) were unmarried,

(47.2%) were married, while the remainder were widowed and divorced. The majority of women (79.6%) were nulliparas, more so in the younger age group (83.9 vs. 53.3). The overall mean parity was ( $0.4 \pm 0.96$ ), and the difference between the two groups was highly significant.  $P = 0.003$ . As to the changes in the menstrual cycle (infrequent), (71.3%) of the enrolled women reported a history of oligomenorrhea followed by (25.9%) hypomenorrhea and (2.8%) with the normal menstrual cycle. Statistically, the differences between the two age groups

were insignificant  $P$ -value  $> 0.05$ . More than one-quarter of the sample (27.8%) reported a history of infertility, (17.6%) primary and (10.2%) secondary. Primary infertility was more common among the younger age group (18.3% vs. 13.3%), unlike secondary infertility, which was more common among the older age group (7.5% vs. 26.7%). The differences were statistically insignificant.  $P$ -value  $> 0.05$ , table 1.

**Table 1: Study Sample by Age and Obstetrical History.**

| Obstetrical History    |           | Age (years) |            |          |            | p*    | Total     |            |
|------------------------|-----------|-------------|------------|----------|------------|-------|-----------|------------|
|                        |           | 15 – 30     |            | 31 – 39  |            |       | (n = 108) |            |
|                        |           | (n = 93)    |            | (n = 15) |            |       |           |            |
|                        |           | No.         | %          | No.      | %          |       | No.       | %          |
| Parity                 | Nil       | 78          | 83.9       | 8        | 53.3       | 0.008 | 86        | 79.6       |
|                        | 1-5       | 15          | 16.1       | 7        | 46.7       |       | 22        | 20.4       |
|                        | Mean ± SD |             | 0.3 ± 0.69 |          | 1.3 ± 1.27 |       | 0.003     | 0.4 ± 0.96 |
| Family history of PCOS |           | 47          | 50.5       | 9        | 60.0       | 0.496 | 56        | 51.9       |
| Oligomenorrhea         |           | 66          | 71.0       | 11       | 73.3       | 1.000 | 77        | 71.3       |
| Normal menstrual cycle |           | 2           | 2.2        | 1        | 6.7        | 1.000 | 3         | 2.8        |
| Hypomenorrhea          |           | 26          | 28.0       | 2        | 13.3       | 0.345 | 28        | 25.9       |
| Infertility            | Primary   | 17          | 18.3       | 2        | 13.3       | 0.088 | 19        | 17.6       |
|                        | Secondary | 7           | 7.5        | 4        | 26.7       |       | 11        | 10.2       |

\* Based on Fisher's exact test, except mean parity on Mann-Whitney test.

The most common clinical finding was generalized alopecia (62.0%) followed by generalized and local hirsutism (44.4% and 41.7% resp.), Acne (19.4%) and Acanthosis (17.6%). None of the comparisons between the two main age groups proved statistically significant.  $P$ -value  $> 0.05$ . Most of the enrolled women were overweight, with the majority (70.6%) falling in the BMI range of 25 - <40.

Those falling in the normal range constituted only 28.7%. Age-wise, the younger and older groups didn't differ significantly across the different levels of BMI.  $p = 0.407$ , table 2.

Table 2: Clinical and U/S Findings by Age

| Clinical Findings        |                                        | Age (years) |      |          |      | p*    | Total     |      |
|--------------------------|----------------------------------------|-------------|------|----------|------|-------|-----------|------|
|                          |                                        | 15 – 30     |      | 31 – 38  |      |       | (n = 108) |      |
|                          |                                        | (n = 93)    |      | (n = 15) |      |       |           |      |
|                          |                                        | No.         | %    | No.      | %    |       | No.       | %    |
| Hirsutism                | Generalized                            | 41          | 44.1 | 7        | 46.7 | 0.678 | 48        | 44.4 |
|                          | Local                                  | 40          | 43.0 | 5        | 33.3 |       | 45        | 41.7 |
| Alopecia                 | Generalized                            | 60          | 64.5 | 7        | 46.7 | 0.380 | 67        | 62.0 |
|                          | Local                                  | 2           | 2.2  | 0        | 0.0  |       | 2         | 1.9  |
| Acanthosis               |                                        | 16          | 17.2 | 3        | 20.0 | 0.725 | 19        | 17.6 |
| Acne                     |                                        | 20          | 21.5 | 1        | 6.7  | 0.294 | 21        | 19.4 |
| BMI (kg/m2)              | < 18.5                                 | 1           | 1.1  | 0        | 0.0  | 0.407 | 1         | 0.9  |
|                          | 18.5 - < 25                            | 28          | 30.1 | 3        | 20.0 |       | 31        | 28.7 |
|                          | 25 - < 30                              | 34          | 36.6 | 4        | 26.7 |       | 38        | 35.2 |
|                          | 30 - < 40                              | 28          | 30.1 | 7        | 46.7 |       | 35        | 32.4 |
|                          | ≥ 40                                   | 2           | 2.2  | 1        | 6.7  |       | 3         | 2.8  |
| Abdominal<br>U/S Finding | Presence of ≥ 12<br>follicles (2-9 mm) | 83          | 90.3 | 10       | 66.7 | 0.007 | 94        | 87.1 |
|                          | Increased ovarian<br>volume (> 10 ml)  | 81          | 86.1 | 10       | 66.7 | 0.013 | 91        | 84.2 |

\* Based on Fisher's exact test.

The most commonly raised hormone was testosterone (21.3%), followed by prolactin (7.4%) and TSH (2.8%). Only (11.1%) exhibited an LH/FSH ratio of  $\geq 3$ .

Age wise, the younger and older groups did not differ significantly neither in hormone levels nor in the LH / FSH ratio.  $p > 0.05$ , table 3.

Table 3: Biochemical Findings by Age

| Biochemical Findings    | Age (years) |         |         |     | P*    | Total (n =108) |      |
|-------------------------|-------------|---------|---------|-----|-------|----------------|------|
|                         | 15 – 30     |         | 31 – 39 |     |       |                |      |
|                         | (n= 93)     | (n= 15) |         |     |       |                |      |
|                         | No.         | %       | No.     | %   |       | No.            | %    |
| Testosterone >0.7 ng/ml | 22          | 23.7    | 1       | 6.7 | 0.184 | 23             | 21.3 |
| Prolactin >35 ng/ml     | 8           | 8.6     | 0       | 0.0 | 0.596 | 8              | 7.4  |
| TSH > 5 mIU/l           | 2           | 2.2     | 1       | 6.7 | 0.364 | 3              | 2.8  |
| LH/FSH ≥ 3              | 11          | 11.8    | 1       | 6.7 | 1.000 | 12             | 11.1 |

\* Based on Fisher's exact test.

Different PCOS features, including hirsutism, cycle disturbance, BMI  $\geq 25$ , and high testosterone level, were compared between patients with and without positive

U/S findings; none of these comparisons achieved statistical significance.  $P$ -value  $> 0.05$ . The same applies to women with LH/FSH  $\geq 3$ , table 4.

Table 4: PCOS Features by U/S Findings.

| PCOS Features       | Positive U/S findings (n = 94) |      | Negative U/S findings (n = 14) |      | p*    | Total (n = 108) |      |
|---------------------|--------------------------------|------|--------------------------------|------|-------|-----------------|------|
|                     | No.                            | %    | No.                            | %    |       | No.             | %    |
| Hirsutism           | 82                             | 87.2 | 11                             | 78.6 | 0.408 | 93              | 86.1 |
| Cycle disturbance** | 93                             | 98.9 | 12                             | 85.7 | 0.538 | 105             | 97.2 |
| BMI 25 – 29         | 66                             | 70.2 | 10                             | 71.5 | 0.926 | 76              | 70.4 |
| BMI ≥ 30            | 32                             | 34.0 | 6                              | 42.9 | 0.557 | 38              | 35.2 |
| High testosterone   | 21                             | 22.3 | 2                              | 14.3 | 0.730 | 23              | 21.3 |
| LH/FSH ≥ 3          | 9                              | 9.6  | 3                              | 21.4 | 0.187 | 12              | 11.1 |

\* All based on *Chi-square* test.

\*\* Cycle disturbance or infrequent cycle (hypomenorrhea + oligomenorrhea)

## DISCUSSION

The most common endocrine disturbance in women of reproductive age is polycystic ovary syndrome. This syndrome is associated with hormonal, biochemical, and psychological consequences, resulting in reduced health-related quality of life<sup>5,6</sup>.

### 1. Obstetrical History and Clinical Findings

The Prevalence of PCOS depends on the adopted diagnostic criteria. The WHO estimates that PCOS affected 116 million women worldwide as of 2010 (3.4% of the population)<sup>7</sup>. Most of the prevalence studies in India reported the Prevalence of PCOS as (9.13% to 36%)<sup>8</sup>.

A family history of PCOS was documented in (51.9%) of women included in this study; such a finding disagrees with those revealed by a study done in India in which the incidence of PCOS among the study population was (21%). This difference may be due to some of the socio-economic factors like lifestyle, eating habits, and obesity<sup>8</sup>.

PCOS is associated with a wide range of menstrual irregularities ranging from regular oligomenorrhea and

hypomenorrhea; they represented about (97.2%) in this study. A study performed in Beijing/ China revealed that (92%) had abnormal menstrual cycle<sup>9</sup>. In another study, approximately (75-85%) of women with PCOS had clinically evident menstrual dysfunction<sup>10</sup>.

Regarding infertility, more than one-quarter of the sample (27.8%) presented with a history of infertility. However, the overall Prevalence of infertility could be higher since (50.9%) of the enrolled women were unmarried; moreover, the married PCOS women are usually under the gynecologist care because of their initial concern of infertility. A study performed in Libya revealed that (40%) had a history of infertility<sup>11</sup>.

In this study, the most common clinical finding was generalized alopecia (62.0%). An earlier study done by Quinn *et al.* reported (22%) prevalence of alopecia in their study population, which is around one-third of the local figure. This may be due to the possibility of a confounding diagnosis such as age-related female-pattern hair loss<sup>12</sup>.

The hirsutism, (86.1%) were having hirsutism in this study, which is a little lower than the findings of an earlier study done in Libya, which revealed that (91%) had hirsutism<sup>11</sup>. This same study revealed that only 12% of patients had acne, in contrast to about 25% reported worldwide. The age factor is playing an important role in this difference<sup>13</sup>.

Obesity is less common in PCOS women of Mediterranean descent but more common in Hispanic, black, and white women with PCOS<sup>14</sup>. This study revealed the overweight effect (67.6%) with a BMI range of 25-<40. This high rate of overweight may indirectly reflect the high prevalence of overweight in our community in general. An earlier study by Najem in Libya revealed that the overweight was (81%) with the BMI range 24-<40, and obesity affecting 57% of Libyan PCOS patients<sup>11</sup>.

The relation between obesity and PCOS is supported by the fact that a lifestyle change and control of weight will decrease PCOS symptoms and correct the hormonal imbalance. Two studies in India concluded that obesity increases the risk of PCOS to a lesser degree; it was seen that 40% of the overweight women suffered from PCOS<sup>15,16</sup>, and the same result (43%) in a study at a tertiary health care hospital in Western Maharashtra by Shinde, et al., (2019)<sup>17</sup>.

In this study, the most common U/S finding was the bilateral presence of  $\geq 12$  follicles (2-9mm) (87.1%) followed by bilateral increased ovarian volume ( $>10$ m) (84.2%). In an earlier study in Libya, the percentage of ultrasonography features of polycystic ovaries was (74%) close to the finding in the current study<sup>11</sup>. It is well known that

trans-abdominal U/S is less sensitive than trans-vaginal U/S<sup>18</sup>. Both previous findings were much less than those reported by others (96.7%) who used transvaginal ultrasound. The underutilization of transvaginal ultrasound is due to cultural and religious restrictions in Muslim societies, and most of the women in this study were unmarried<sup>14</sup>.

## 2. Biochemical Findings

The most common raised hormone in this study was testosterone (21.3%), which was a little lower than the finding in an earlier study in Libya which was (26%)<sup>11</sup>. The low rate of elevated testosterone in the study sample seems to be an underestimate to the actual rate of biochemical hyperandrogenism because the results depend on total serum testosterone assays rather than free testosterone assays according to availability issues<sup>19</sup>.

The high frequency of hyperprolactinemia (31%) observed in Libian patients is worth investigating by using multiple sample measurements at a different time; this finding disagrees with the current study in which the prolactin level was mildly elevated in (7.4%) only. The LH/FSH ratio of  $\geq 3$  constituted (11%) compared to (16%) reported by a previous study in Libya<sup>11</sup>, this is an indicator for the low sensitivity of this test as a diagnostic tool in this context, but many researchers consider that about 30 % of women with PCOS had LH / FSH ratio  $\geq 3:1$ , and this ratio is diagnostic for this syndrome<sup>11</sup>.

## CONCLUSIONS

In local practice, menstrual abnormalities, mostly as hypomenorrhea and oligomenorrhea, constituted the most common presentation. On the other hand,

the concurrent presence of hyperandrogenism and positive ultrasound findings were more stable features and may be suggested as a better indicator for establishing the diagnosis of the syndrome locally. A more extended study, including bigger sample size, is suggested to verify the conclusions of this study and detect a more valid characterization of PCOS's local pattern.

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## پوخته

## متلازمة تكيس المبايض في دهوك تحديد الخصائص السريرية والكيميائية

## پیشهکی

(متلازمة المبايض المتعدد الكيسات) لقینه کا ئالوز و نه ریک و پیکه کارتیکنی دکه ته سه 5% 10 ژ ئافره تان ل ژیی زاروک بوونی، ئه فه ژی دبیه ئه گهری ده رکه فتنا کیم سیین دوینده هی و هیکا و غودی و نه زوکی و خراب بوونا ئه ندروجینی و قه له وی و خراب بوونا ئه نسولینی و زیده بوونا مه ترسیا تو شبوونا ژ جوری DM2 و نه خوشین دلی و ده مارین خویی. دیارکنا ئه گهر و گریین لوجستی ژ سه ربورا دوماهی لده ف مروقی بو ده ستیشانکنا ئه گهری.

## نارمانج

ده ستین شانکنا سالوخه تین ته ختی و کیمیایی بین زیندی و جفاکی و دیموگرافی یه بو نه خو شین (متلازمة المبايض المتعدد الكيسات) ل دهوکی. و به راوردکنا ئان فان ئه نجامان دگه ل هه مان وان زانیاریین هاتینه کومکرن ل ده قهرین دی.

## ئه نجام

ئه نجام نافه ئافره تین گرییدی 24.3+5.54 دناقه را 15-39. و زوربه یا وان (81.5%) خار ژیی 30 سالیی بوون. حاله تین پتر به ره بلاف ژ فی نه خوشیی (35.2%) دناقه را ژیی 20 و 24 سالییدا بوون. ئاستی فیژیوونا خاندنا نافنجی و زانکویی گه هشته (68.5%) و (50.9%) کچ بوون. و خیزانین میژوویا فی نه خو شیی لده ف وان هه ی (51.9%) بوون. بتنی (2.8%) ژ وان چاره سه ریین دلی و نه خو شیین دوم دریز بکار دئیان. نه ریک و پیکیا خولا هه یقانه لده ف (97.2%) ژ وانا هه بوو و (27.8%) ژ وان میژوویا نه زوکی هه بوو. ئه نجامی ته ختی یی هه ره به ره بلاف (معمة والشعرانية المحلية) بوون ب ریژا (86.1%) و لدویفا می وه ریان ب ریژا (62.0%) و (21.3%) ئاستی هورمونی تستسترون لده ف وان یی بلند بوو.

## ده رئه نجام

قه کولینه کا پارچه یی یه، پشکدار و ریک: ئه ف قه کولینا ل به رچا هاته کرن ل نه خوشخانا دهوک ئازادی یا فیترکرنی پشکا کلینیکی ژده رقه بو نه خو شیین ئافره ت و زاروک بوونی و پشکا کلینیکی ژده رقه بو نه خو شیین ئافره ت و زاروک بوونی ل نه خو شخانا زاخو یا ئافره ت و زاروک بوونی و کومه لگه ها نوژداری ل زاخو، ل هه ریما کوردستانا عیراقی، د ماوه یی ژ مه ها ته موز تا کانوینا ئیکی یا سالا 2019. لسه ر بنیاتی میژوویا نه خو شی و میژوویا نوژداری و میژوویا نه خو شیین ئافره ت و پشکینا ته ختی و پشکینا تاقیگه هی و هه ل سه نگاندنا تیشکی (پیلین سه ر و ده نگی)، هه قدیتن و پشکینا 108 نه خوشان هاته کرن ژلایی قه کولهری قه بو زانین و پشت راستکنا زانیاریین ژئی هاتینه داخواز کرن لدویف پرسپار ناما باوه ر پیکری.

## الخلاصة

### متلازمة تكيس المبايض في دهوك تحديد الخصائص السريرية والكيميائية

#### خلفية البحث

ان متلازمة تكيس المبايض اضطراب معقد وغير متجانس يصيب 5-10٪ من النساء في سن الإنجاب، مما يتسبب في مجموعة من عيوب الإنجاب والأبيض والغدد الصماء التي تتميز بعدمالأباضة المزمنة، وفرط الأندروجينية وتكيس المبايض. تتجلى المتلازمة بأشكال مختلفة اعتماداً على العديد من العوامل المتفاعلة، بما في ذلك التعرض البيئي، وعوامل الوراثة، وأسلوب الحياة. تهدف هذه الدراسة إلى تحديد صفات المتلازمة لدى النساء في دهوك.

#### المرضى وطرق البحث

تم إجراء هذه الدراسة المقطعية خلال الفترة من يونيو إلى ديسمبر 2019، في مستشفى آزادي التعليمي/ دهوك، بالإضافة إلى أقسام العيادات الخارجية في مستشفى زاخو للولادة ومجمع كردستان الطبي. قام الباحث بإجراء مقابلات مع 108 مرضى مؤهلين وفقاً لمعايير روتردام ESHRE / ASRM لفحص وتوثيق البيانات المطلوبة وفقاً للاستبيان المعتمد الذي تضمن التاريخ المرضي والفحص السريري والفحص المختبري والموجات فوق الصوتية للبطن. تم استخدام الحزمة الإحصائية SPSS الإصدار 19 لتحليل متغيرات الدراسة وكانت الاختبارات الإحصائية المستخدمة هي: مربع Chi، واختبار-Man Whitney، وUnpaired t-test.

#### النتائج

كان متوسط عمر النساء  $24.3 \pm 5.54$  والأغلبية دون 30 سنة مع زيادة عن المعدل المقبول للوزن، وكان (50.9%) غير متزوجات و(68.5%) لديهن مستويات تعليم ثانوي/ جامعي مع (51.9%) ممن لديهن تاريخ أسري للإصابة بالمتلازمة و(2.8%) ممن لهن تاريخ مرضي يخص الأمراض القلبية الوعائية والأبيض واستخدام الأدوية المزمنة. تم تثبيت اضطرابات الدورة الشهرية لدى (97.2%) والعقم في (27.8%) كما كانت العلامات الأكثر شيوعاً هي الشعورية تليها الصلع واسع الانتشار وارتفاع مستوى التستوستيرون. تم الكشف عن تكيس المبايض في (75.3%) باستخدام فحص U/S وكان تكيس كلا المبايض أكثر تواتراً في الفئة العمرية الأصغر سناً.

#### الاستنتاجات

أغلبية النساء كان لديهن اضطرابات في الدورة الشهرية مثل نقص وشحة الطمث. من ناحية أخرى، كان الوجود المتزامن لفرط الأندروجينية ونتائج الموجات فوق الصوتية الإيجابية ميزات أكثر استقراراً ويمكن اقتراحها كمؤشر أفضل لتحديد تشخيص المتلازمة محلياً.