**Supplementary Files**

**Supplementary Table 1**. Reference values of endocrine and metabolic test.

|  |  |
| --- | --- |
|  | Reference value |
| FSH (mUl/ml) | Follicular phase: 3.5-12 .5 |
| Luteal phase: 1.7-7.7 |
| Ovulatory phase: 4.7-21.5 |
| Post menopause: 25.8-134.8 |
| AMH (ng/ml) | Optimal Fertility: 4.0-6.8 |
| Satisfactory fertility: 2.2-4.0 |
| Low fertility: 0.3-2.2 |
| Undetectable or very low: 0.0-0.3 |
| High Level: > 6.8 |
| LH (mUl/ml) | Follicular phase: 2.4-12.6 |
| Luteal phase: 1.0-11.4 |
| Ovulatory phase: 14.0-95.6 |
| Post menopause: 7.7-58.5 |
| TSH (mUl/ml) | 0.39-6.16 |
| E2 (pg/ml) | Follicular phase: 9.0-175 |
| Luteal phase: 44.0-196 |
| Ovulatory phase: 107-281 |
| Post menopause: < 0.5 -20 |
| Free testosterone (pg/ml) | 0.01-7.01 |
| Fasting insulin (uUl/ml) | 2-25 |
| Post meal insulin (uUl/ml) | 0-60 |
| Fasting blood glucose (mg/dL) | 70-105 |
| Androstenedione (ng/ml) | Follicular phase: 0.5 - 4.7 |
| Ovulatory peak: 0.9 - 3.0 |
| Luteal phase: 0.9 - 4.7 |
| DHEAS (ug/dL) | 30 - 280 |
| Glycosylated hemoglobin (%) | Patient: Non-Diabetic 4.0-6.5 |
| Objective: 6.5-7.0 |
| Good Control: 7.0-8.0 |
| Accurate Performance: > 8.0 |

*Abbreviations:* FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate. ***Clarification:*** This research derived from a project macro whose objective was to analyze in 98 Colombian women (controls (n=49) and PCOS patients (n=49)) different polymorphisms associated with PCOS risk, which are located in 11 different genes. Thus, the research reported in this manuscript uses the same sample of controls (n=49) and PCOS patients (n=49), clinical data, and methodology for data analysis. Therefore, the materials and methods section, clinical and endocrine characteristics of subjects, clinical measurements, endocrine and metabolic evaluation, DNA isolation and genotyping, and statistical analysis are common to all reports derived from this macro project.

**Supplementary Table 2**. MassArray design details for variants in the *LHCGR* gene.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP\_ID** | **TERM** | **2nd-PCRP** | **1st-PCRP** | **AMP\_LEN** | **UP\_CONF** | **MP\_CONF** | **Tm (NN)** | **PcGC** | **UEP\_DIR** | **UEP\_MASS** | **UEP\_SEQ** | **EXT1\_CALL** | **EXT1\_MASS** | **EXT1\_SEQ** | **EXT2\_CALL** | **EXT2\_MASS** | **EXT2\_SEQ** |
| rs13405728 | iPLEX | ACGTTGGATGCTTCAATATCCTGGGCTTAC | ACGTTGGATGGATTTAGAAACCTGCTCTGG | 120 | 95.6 | 72.3 | 49.2 | 42.1 | R | 5762.8 | CCATAATGCAGCCATTTGT | G | 6010.0 | CCATAATGCAGCCATTTGTC | A | 6089.9 | CCATAATGCAGCCATTTGTT |
| rs7371084 | iPLEX | ACGTTGGATGCAGTCCCACTATTTAACAGC | ACGTTGGATGCAAGCCTATTATTGGATCCAT | 120 | 85.2 | 72.3 | 47.7 | 38.1 | R | 7634.0 | agacGCAAGTTACTTAACCGATCTA | T | 7905.2 | agacGCAAGTTACTTAACCGATCTAA | C | 7921.2 | agacGCAAGTTACTTAACCGATCTAG |
| rs4953616 | iPLEX | ACGTTGGATGACTTCATCAGCCACTCTATG | ACGTTGGATGCTACATAACCACACTGAGGG | 116 | 97.6 | 72.3 | 47.1 | 34.8 | F | 6868.5 | CCTCATCATCATTTCCATTATAC | C | 7115.7 | CCTCATCATCATTTCCATTATACC | T | 7195.6 | CCTCATCATCATTTCCATTATACT |
| rs2293275 | iPLEX | ACGTTGGATGCAATGTGAAAGCACAGTAAG | ACGTTGGATGCACACAGAACAAGATACGAC | 111 | 92.6 | 72.3 | 47.1 | 44.4 | R | 5934.9 | gGCACAGTAAGGAAAGTGA | T | 6206.1 | gGCACAGTAAGGAAAGTGAA | C | 6222.1 | gGCACAGTAAGGAAAGTGAG |
| rs6732721 | iPLEX | ACGTTGGATGGACATAGCAGGAGTTGTCAG | ACGTTGGATGTTCCTGTCACTCCATCGTTG | 90 | 99.6 | 72.3 | 45.7 | 40.0 | R | 7152.7 | cggTGTCAGGAAGAGTAATCTAG | T | 7423.9 | cggTGTCAGGAAGAGTAATCTAGA | C | 7439.9 | cggTGTCAGGAAGAGTAATCTAGG |

Abbreviations: TERM: Termination chemistry; SNP\_ID: Reference of the sequence; 2nd-PCRP: First Forward Sequence; 1st-PCRP: First Reverse Sequence; AMP\_LEN: Length of the amplicon; UP\_CONF: Uniplex Amplification Score (this score indicates how well the amplicon meets the design criteria, individually); MP\_CONF: multiplex amplification score (this score indicates how well the amplicon meets the design criteria, taking into account the other primers included in the multiplex reaction); Tm (NN): Melting temperature for the extension primer; PcGC: Percentage of GC contained in the first extension; UEP\_DIR: Address of the extension first; UEP\_MASS: Mass of the first extension; UEP\_SEQ: Sequence of extension first; EXT1\_CALL: First allelic variant; EXT1\_MASS: Mass of the sequence of the first extension + genotype of the first allelic variant; EXT1\_SEQ: Sequence of the first extension + first allelic variant; EXT2\_CALL: Second allelic variant; EXT2\_MASS: Mass of the sequence of the first extension + genotype of the second allelic variant; EXT2\_SEQ: Sequence of the first extension + second allelic variant.

**Supplementary Table 3.** SNPs genotyped in the *LHCGR* gene.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| db SNP ID | Chromosome location | Nucleotide change | Type | MAFa |
| rs13405728 | chr2:48751020  | A→G | Intron variant; genic downstream transcript variant; genic upstream transcript variant | 0.21 |
| rs7371084 | chr2:48712814 | T→C | Intron variant; genic downstream transcript variant; genic upstream transcript variant | 0.13 |
| rs4953616 | chr2:48714289 | T→C | Intron variant; genic downstream transcript variant; genic upstream transcript variant | 0.32 |
| rs2293275 | chr2: 48694236 | C→T | Missense variant; coding sequence variant; upstream transcript variant; genic downstream transcript variant | 0.4 |
| rs6732721 | chr2:48738464 | T→C | Intron variant; genic downstream transcript variant; genic upstream transcript variant | 0.27 |

aMinor allele frequency according to 1000 Genomes Project **(available in** [**https://www.ncbi.nlm.nih.gov/snp/**](https://www.ncbi.nlm.nih.gov/snp/)**)**

**Supplementary Table 4.** Clinical and endocrine-metabolic parameters of women with PCOS according to the dominant model of rs13405728 in *LHCGR* gene.

|  |  |
| --- | --- |
|  | rs13405728 |
|  | **AA****(n=40)** | **GA+GG****(n=9)** | **P-value** |
| Age (years) | 28 (24-32) | 30 (22.5-34.5) | 0.826† |
| Weight (kg) | 59.5 (55-71.75) | 65 (55.5-77.5) | 0.596† |
| Height (m) | 1.62 (1.58-1.66) | 1.63 (1.62-1.66) | 0.551† |
| BMI (kg/m2) | 23.15 (21.48-25.31) | 23.5 (21.14-30.13) | 0.846† |
| Menarche (years) | 13 (12-14) | 13 (12-14) | 0.968† |
| Menstrual cycle (days) | 31 (30-45) | 30 (22-43.5) | 0.22† |
| Menstrual cycle length (days) | 5 (4-8) | 5 (2.5-7.5) | 0.402† |
| FSH (mUl/ml) | 5.81 (2.8-8.83) | 4.9 (2.02-9.26) | 0.486† |
| AMH (ng/ml) | 8.31 (5.13-13.1) | 6.16 (4.26-10.48) | 0.278† |
| LH (mUl/ml) | 7.15 (4.79-11.47) | 5 (1.98-5.56) | **0.013**† |
| LH/FSH ratio | 1.39 (1.03-1.78) | 0.85 (0.37-1.20) | **0.014**† |
| TSH (mUl/ml) | 1.7 (1.29-2.69) | 1.63 (1.32-3.28) | 0.776† |
| E2 (pg/ml) | 52.1 (28.8-72.85) | 65.9 (51.8-122) | 0.282† |
| Androstenedione (ng/ml) | 1.5 ± 0.61 | 1.54 ± 0.54 | 0.837†† |
| DHEAS (ug/dL) | 154.05 ± 61.46 | 157 ± 77.99 | 0.902†† |
| Free testosterone (pg/ml) | 1.36 (0.89-2.55) | 1.32 (0.94-1.96) | 0.99† |
| Fasting insulin (uUl/ml) | 4.64 (2.61-8.6) | 7.26 (2.17-10.81) | 0.644† |
| Post meal insulin (uUl/ml) | 27.6 (12.25-44.35) | 36.4 (19.75-45.05) | 0.434† |
| Fasting blood glucose (mg/dL) | 82.56 ± 8.44 | 89.46 ± 7.03 | **0.028**†† |
| Post meal glucose (mg/dL) | 80 (68.5-94.5) | 81 (73-95.5) | 0.727† |
| HOMA-IR | 0.72 (0.42-1.56) | 1.63 (0.47-2.64) | 0.511† |
| HOMA-IS | 0.052 (0.026-0.08) | 0.029 (0.016-0.094) | 0.521† |
| Glycosylated hemoglobin (%) | 5.2 (5-5.52) | 5.5 (5.17-6.06) | 0.163† |
| Total ovarian volume (cm3) | 13.8 (9.7-19.5) | 11.55 (7.82-14.45) | 0.21† |
| Total AFC (number of follicles) | 28.5 (23.25-35) | 25 (15.5-28.5) | 0.11† |

*Abbreviations*: BMI: Body mass index; FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance; HOMA-IS: Homeostasis Model Assessment-Insulin Sensitive; AFC: Antral follicular count.

†Mann-Whitney U-test (no-continuous variables). Data are expressed as median (interquartile range).

††Student's t-test (continuous variables). Data are expressed as mean ± standard deviation.

**Supplementary Table 5.** Clinical and endocrine-metabolic parameters of women with PCOS according to the overdominant model of rs7371084 in *LHCGR* gene.

|  |  |
| --- | --- |
|  | rs7371084 |
|  | **TT+CC****(n=38)** | **TC****(n=11)** | **P-value** |
| Age (years) | 28 (23.75-32.25) | 28 (22-33) | 0.943† |
| Weight (kg) | 62.5 (55-73.5) | 59 (55-87) | 0.719† |
| Height (m) | 1.62 (1.58-1.67) | 1.62 (1.62-1.63) | 1† |
| BMI (kg/m2) | 23.37 (21.65-25.49) | 21.83 (19.95-32.75) | 0.415† |
| Menarche (years) | 13 (12-14) | 13 (13-14) | 0.417† |
| Menstrual cycle (days) | 31 ( 30-36.75) | 38 (28-78.75) | 0.540† |
| Menstrual cycle length (days) | 5 (3.75-8) | 5 (4-7) | 0.568† |
| FSH (mUl/ml) | 6.17 (3.43-8.83) | 3.36 (1.81-11.2) | 0.260† |
| AMH (ng/ml) | 7.52 (4.90-11.7) | 10.7 (5.39-14.7) | 0.270† |
| LH (mUl/ml) | 7.15 (5.3-10.65) | 3.32 (1-6.93) | **0.020**† |
| LH/FSH ratio | 1.36 (0.93-1.87) | 1.11 (0.47-1.47) | 0.069† |
| TSH (mUl/ml) | 1.74 (1.33-2.98) | 1.55 (1.24-2.49) | 0.332† |
| E2 (pg/ml) | 59.3 (31.8-122) | 45.5 (34.15-62.95) | 0.302† |
| Androstenedione (ng/ml) | 1.49 ± 0.56 | 1.55 ± 0.72 | 0.778†† |
| DHEAS (ug/dL) | 152.39 ± 57.88 | 162.18 ± 84.43 | 0.724†† |
| Free testosterone (pg/ml) | 1.34 (0.94-2.3) | 1.68 ( 0.69-4.49) | 0.857† |
| Fasting insulin (uUl/ml) | 4.97 (2.35-8.57) | 4.72 (2.7-11) | 0.836† |
| Post meal insulin (uUl/ml) | 25.1 (13.3-40.9) | 33.2 (19.6-55.6) | 0.258† |
| Fasting blood glucose (mg/dL) | 83.6 ± 8.62 | 84.6 ± 8.77 | 0.739†† |
| Post meal glucose (mg/dL) | 80 (72.15-93) | 86 (71-101) | 0.494† |
| HOMA-IR | 0.99 (0.53-1.77) | 0.85 (0.53-2.44) | 0.814† |
| HOMA-IS | 0.044 (0.025-0.083) | 0.05 (0.01-0.08) | 0.814† |
| Glycosylated hemoglobin (%) | 5.34 (4.97-5.89) | 5.16 (5.08-5.5) | 0.563† |
| Total ovarian volume (cm3) | 12.19 (9.62-19.13) | 13.2 (9.23-17.59) | 0.980† |
| Total AFC (number of follicles) | 27 (23 (34) | 31 (24-36) | 0.667† |

*Abbreviations*: BMI: Body mass index; FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance; HOMA-IS: Homeostasis Model Assessment-Insulin Sensitive; AFC: Antral follicular count.

†Mann-Whitney U-test (no-continuous variables). Data are expressed as median (interquartile range).

††Student's t-test (continuous variables). Data are expressed as mean ± standard deviation.

**Supplementary Table 6.** Clinical and endocrine-metabolic parameters of women with PCOS according to the overdominant model of rs4953616 in *LHCGR* gene.

|  |  |
| --- | --- |
|  | rs4953616 |
|  | **TT+CC****(n=26)** | **CT****(n=23)** | **P-value** |
| Age (years) | 28 (23.75-33.5) | 27 (23-31) | 0.434† |
| Weight (kg) | 62.5 (55.75-75.5) | 59 (55-75) | 0.652† |
| Height (m) | 1.62 (1.58-1.65) | 1.63 (1.60-1.67) | 0.398† |
| BMI (kg/m2) | 23.2 (22.13-25.23) | 22.49 (19.95-28.23) | 0.477† |
| Menarche (years) | 13 (12-14) | 13 (12-14) | 0.910† |
| Menstrual cycle (days) | 31 (30-45) | 31 (28-39) | 0.681† |
| Menstrual cycle length (days) | 5 (4-8) | 5 (4-8) | 0.707† |
| FSH (mUl/ml) | 6.03 (3.16-8.64) | 5.52 (2.24-9.58) | 0.928† |
| AMH (ng/ml) | 6.75 (4.78-9.06) | 12 (5.15-16.2) | **0.030**† |
| LH (mUl/ml) | 6.85 (4.57-11.52) | 6.8 (3.32-9) | 0.631† |
| LH/FSH ratio | 1.37 (0.82-1.87) | 1.21 (0.85-1.58) | 0.459† |
| TSH (mUl/ml) | 1.77 (1.29-2.78) | 1.62 (1.27-2.63) | 0.711† |
| E2 (pg/ml) | 64.4 (32.55-98.95) | 48.3 (31.8-68) | 0.362† |
| Androstenedione (ng/ml) | 1.55 ± 0.49 | 1.46 ± 0.7 | 0.615†† |
| DHEAS (ug/dL) | 139.57 ± 58.17 | 171.56 ± 67.07 | 0.080†† |
| Free testosterone (pg/ml) | 1.47 (0.84-2.86) | 1.32 (0.98-2) | 0.904† |
| Fasting insulin (uUl/ml) | 3.94 (2.31-6.19) | 8.21 (2.93-11.07) | 0.050† |
| Post meal insulin (uUl/ml) | 27.6 (13.35-41.15) | 29.9 (13.7-45.8) | 0.489† |
| Fasting blood glucose (mg/dL) | 83.61 ± 8.98 | 84.07 ± 8.27 | 0.852†† |
| Post meal glucose (mg/dL) | 84 (74-93.5) | 78 (71-96) | 0.802† |
| HOMA-IR | 0.73 (0.5-1.29) | 1.52 (0.58-2.64) | 0.080† |
| HOMA-IS | 0.061 (0.03-0.08) | 0.029 (0.016-0.07) | 0.078† |
| Glycosylated hemoglobin (%) | 5.2 (4.96-5.45) | 5.34 (5.09-6.05) | 0.103† |
| Total ovarian volume (cm3) | 14.98 (11.68-22.76) | 11.1 (8.11-15.67) | **0.026**† |
| Total AFC (number of follicles) | 27 (23-34.5) | 31 (23-35) | 0.811† |

*Abbreviations*: BMI: Body mass index; FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance; HOMA-IS: Homeostasis Model Assessment-Insulin Sensitive; AFC: Antral follicular count.

†Mann-Whitney U-test (no-continuous variables). Data are expressed as median (interquartile range).

††Student's t-test (continuous variables). Data are expressed as mean ± standard deviation.

**Supplementary Table 7.** Clinical and endocrine-metabolic parameters of women with PCOS according to the recessive model of rs2293275 in *LHCGR* gene.

|  |  |
| --- | --- |
|  | rs2293275 |
|  | **CC+TC****(n=43)** | **TT****(n=6)** | **P-value** |
| Age (years) | 28 (23-32) | 31.5 (23.5-34.5) | 0.445† |
| Weight (kg) | 64 (53-67) | 56 (51.5-61) | 0.067† |
| Height (m) | 1.63 (1.60-1.67) | 1.61 (1.55-1.66) | 0.462† |
| BMI (kg/m2) | 23.23 (21.48-26.18) | 21.61 (19.96-24.75) | 0.161† |
| Menarche (years) | 13 (12-14) | 13 (11.75-14.25) | 0.888† |
| Menstrual cycle (days) | 31 (28-45) | 36 (35-36) | 0.102† |
| Menstrual cycle length (days) | 5 (4-8) | 5 (3.75-5.75) | 0.781† |
| FSH (mUl/ml) | 5.66 (2.57-8.87) | 5.15 (2.97-8,67) | 0.760† |
| AMH (ng/ml) | 8.02 (5.11-12.6) | 7.94 (3.91-12.62) | 0.714† |
| LH (mUl/ml) | 6.7 (4.6-11.4) | 7.55 (1.45-8.78) | 0.604† |
| LH/FSH ratio | 1.31 (0.96-1.76) | 0.83 (0.53-1.59) | 0.180† |
| TSH (mUl/ml) | 1.75 (1.34-2.86) | 1.34 (1.04-1.93) | 0.116† |
| E2 (pg/ml) | 53.3 (32.72-72.87) | 50.15 (29.6-117.57) | 0.870† |
| Androstenedione (ng/ml) | 1.54 ± 0.61 | 1.26 ± 0.43 | 0.283†† |
| DHEAS (ug/dL) | 157.18 ± 66.12 | 136 ± 44.81 | 0.453†† |
| Free testosterone (pg/ml) | 1.36 (0.94-2.42) | 0.95 (0.59-1.89) | 0.211† |
| Fasting insulin (uUl/ml) | 4.72 (2.7-9.95) | 4.24 (2-7.49) | 0.375† |
| Post meal insulin (uUl/ml) | 26.7 (11.72-40.6) | 39.45 (24.6-52.95) | 0.184† |
| Fasting blood glucose (mg/dL) | 84.15 ± 8.24 | 81.5 ± 11.3 | 0.483†† |
| Post meal glucose (mg/dL) | 80 (73-93) | 85.5 (64.25-97.75) | 0.951† |
| HOMA-IR | 0.94 (0.55-2.17) | 0.85 (0.41-1.64) | 0.428† |
| HOMA-IS | 0.04 (0.02-0.08) | 0.05 (0.027-0.10) | 0.428† |
| Glycosylated hemoglobin (%) | 5.3 (5.09-5.74) | 4.99 (4.79-6) | 0.344† |
| Total ovarian volume (cm3) | 13.05 (9.67-19.08) | 10.85 (9.08-15.07) | 0.436† |
| Total AFC (number of follicles) | 28.5 (24.25-35) | 23.5 (20.75-34.25) | 0.265† |

*Abbreviations*: BMI: Body mass index; FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance; HOMA-IS: Homeostasis Model Assessment-Insulin Sensitive; AFC: Antral follicular count.

†Mann-Whitney U-test (no-continuous variables). Data are expressed as median (interquartile range).

††Student's t-test (continuous variables). Data are expressed as mean ± standard deviation.

**Supplementary Table 8.** Clinical and endocrine-metabolic parameters of women with PCOS according to the additive model of rs6732721 in *LHCGR* gene.

|  |  |
| --- | --- |
|  | rs6732721 |
|  | **TT****(n=38)** | **CT****(n=10)** | **CC****(n=1)** | **P TT and CT** | **P TT and CC** | **P CT and CC** |
| Age (years) | 28 (24-32.25) | 26.5 (21.75-30.75) | 36 | 0.516† | 0.247† | 0.204† |
| Weight (kg) | 59 (55-73.5) | 64.5 (59-76.25) | 55 | 0.525† | 0.350† | 0.206† |
| Height (m) | 1.62 (1.57-1.67) | 1.63 (1.62-1.65) | 1.62 | 0.467† | 0.964† | 0.416† |
| BMI (kg/m2) | 23.2 (21.48-25.36) | 23.32 (22.2-29.18) | 20.95 | 0.694† | 0.328† | 0.206† |
| Menarche (years) | 13 (12-14) | 12.5 (12-14) | 13 | 0.576† | 0.927† | 0.743† |
| Menstrual cycle (days) | 31 (30-45) | 30 (24-40.5) |   | 0.166† | NC | NC |
| Menstrual cycle length (days) | 5 (4-8) | 4 (2.75-7.25) | 5 | 0.122† | 1 | 0.631† |
| FSH (mUl/ml) | 5.81 (2.69-9.04) | 5.59 (2.13-9.04) | 3.36 | 0.576† | 0.477† | 0.527† |
| AMH (ng/ml) | 8.4 (5.34-13.47) | 5.65 (4.13-9.42) | 3.74 | 0.110† | 0.131† | 0.343† |
| LH (mUl/ml) | 7.15 (4.74-11.45) | 5.41 (2.61-6.85) | 1.6 | 0.082† | 0.131† | 0.206† |
| LH/FSH ratio | 1.33 (0.94-1.76) | 1.03 (0.49-1.66) | 0.48 | 0.148† | 0.110† | 0.343† |
| TSH (mUl/ml) | 1.7 (1.28-2.78) | 1.98 (1.53-2.95) | 1.08 | 0.509† | 0.183† | 0.206† |
| E2 (pg/ml) | 52.1 (28-72.8) | 68.75 (52.02-127.25) | 41 | 0.105† | 0.736† | 0.121† |
| Androstenedione (ng/ml) | 1.49 ± 0.62 | 1.62 ± 0.48 | 1.09 | 0.531†† | 0.532†† | 0.322†† |
| DHEAS (ug/dL) | 151.1 ± 59.49 | 172.6 ± 81.06 | 107 | 0.352†† | 0.469†† | 0.460†† |
| Free testosterone (pg/ml) | 1.47 (0.85-2.62) | 1.3 (0.96-1.94) | 0.91 | 0.859† | 0.424† | 0.267† |
| Fasting insulin (uUl/ml) | 4.68 (2.91-8.67) | 7.26 (2.47-10.81) | 2 | 0.576† | 0.155† | 0.173† |
| Post meal insulin (uUl/ml) | 27.95 (13.32-44.72) | 36.4 (12.43-45.05) | 35.3 | 0.975† | 0.60† | 0.862† |
| Fasting blood glucose (mg/dL) | 82.27 ±8.46 | 88.92 ± 7.17 | 92 | **0.028**†† | 0.264†† | 0.692†† |
| Post meal glucose (mg/dL) | 80 (71.5-93.5) | 79.5 (70.65-96.5) | 95 | 0.970† | 0.350† | 0.527† |
| HOMA-IR | 0.84 (0.46-1.68) | 1.63 (0.53-2.64) | 0.45 | 0.467† | 0.270† | 0.245† |
| HOMA-IS | 0.049 (0.026-0.079) | 0.029 (0.016-0.082) | 0.098 | 0.478† | 0.270† | 0.245† |
| Glycosylated hemoglobin (%) | 5.23 (5.01-5.57) | 5.28 (5.01-5.99) | 5.77 | 0.666† | 0.328† | 0.527† |
| Total ovarian volume (cm3) | 13.8 (9.83-19.25) | 11.22 (7.12-17.12) | 12.5 | 0.185† | 0.964† | 0.527† |
| Total AFC (number of follicles) | 30 (23.75-35.25) | 25 (17-28) | 14 | **0.031**† | 0.103† | 0.115† |

*Abbreviations*: BMI: Body mass index; FSH: Follicle-stimulating hormone; AMH: Anti-Müllerian hormone; LH: Luteinizing hormone; TSH: Thyroid-Stimulating hormone; E2: Estradiol; DHEAS: Dehydroepiandrosterone sulfate; HOMA-IR: Homeostasis Model Assessment-Insulin Resistance; HOMA-IS: Homeostasis Model Assessment-Insulin Sensitive; AFC: Antral follicular count.

†Mann-Whitney U-test (no-continuous variables). Data are expressed as median (interquartile range).

††Student's t-test (continuous variables). Data are expressed as mean ± standard deviation.

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**Supplementary Figure 1.** Degree of linkage disequilibrium (LD) between rs2293275, rs7371084, rs4953616, rs6732721, and 13405728 polymorphisms of *LHCGR* gene, explored in LDlink website (https://ldlink.nci.nih.gov/) in a dataset of 188 Colombians subjects from Medellin, Colombia.