Physical Education, Health and Social Sciences

https://journal-of-social-education.org

E-ISSN: 2958-5996

P-ISSN: 2958-5988

Diagnostic Significance of FSH/LH Ratio in Women Presenting with Infertility

Muhammad Waqas[1], Abdul Rehman[1], Asima Bibi[1], Sobia Latif[1], Muhammad Zain[1], Nadeem Sharif[2]*, Waqas Ahmad[3]

[1] Department of Allied Health Sciences, University of Okara, Okara, Pakistan

[2] Department of Pathology, Isfandyar Bukhari District Hospital Attock, Punjab, Pakistan

Corresponding Author, Email: nadeemsharif59@gmail.com

[3] Department of Allied Health Sciences, Lahore University of Biological & Applied Sciences (UBAS), Lahore, Pakistan

DOI: https://doi.org/10.63163/jpehss.v4i1.1771

Abstract

Routine fertility workups rely heavily on basal serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) assays, yet inspecting either hormone in isolation frequently overlooks subtle hypothalamic-pituitary-ovarian (HPO) axis discordance. We evaluated the statistical distribution, age-related behavior, and clinical classification utility of the serum FSH/LH ratio and its reciprocal (LH/FSH) among women presenting with infertility in Okara, Pakistan. A cross-sectional analytical study was conducted on 80 women presenting with primary or secondary infertility at the Department of Allied Health Sciences (Medical Lab Technology), University of Okara. Venous serum concentrations of LH and FSH (mIU/mL) were quantified by automated chemiluminescence immunoassay. Gaussian normality was evaluated via the Shapiro–Wilk test, rank correlations were estimated using Spearman's rho (ρ), and differences across maternal age brackets (≤24, 25–34, and ≥35 years) were examined by the Kruskal–Wallis test. A total of 80 women presenting with infertility were included in the analysis. The mean age of participants was 30.10 ± 7.00 years, with an age range of 17–48 years. Mean serum LH and FSH concentrations were 16.21 ± 19.72 mIU/mL (median 10.16; IQR 5.45–18.37 mIU/mL) and 17.08 ± 14.07 mIU/mL (median 12.83; IQR 7.36–21.81 mIU/mL), respectively. The mean FSH/LH ratio was 1.87 ± 2.13, with a median of 1.50 (IQR 1.00–2.17) and a range of 0.14–13.64. Shapiro–Wilk testing demonstrated non-normal distributions for LH, FSH and FSH/LH ratio ($p < 0.001$ for each). Spearman correlation analysis showed a weak positive association between age and FSH/LH ratio ($\rho = 0.201$, $p = 0.073$), which was not statistically significant. Absolute serum FSH, however, correlated significantly with age ($\rho = 0.234$, $p = 0.037$) and varied across age brackets (Kruskal–Wallis $H = 6.530$, $p = 0.038$). Ratio thresholds divided the cohort into LH-predominant (FSH/LH < 1.0; 41.3%), concordant (1.00–2.00; 28.8%), and diminished ovarian reserve (FSH/LH > 2.00; 30.0%) profiles, unmasking polycystic ovary syndrome (PCOS) gonadotropin inversion (LH/FSH ≥ 2.0) in 35.5% of women who had normal basal FSH (≤10.0 mIU/mL). Opposing gonadotropin shifts in young anovulatory patients versus older ovarian-depleted patients mute the linear correlation between age and the FSH/LH ratio. Reporting both FSH/LH and LH/FSH ratios alongside raw hormone values sharpens routine laboratory stratification without adding assay cost.

Keywords: *Female Infertility; Fsh/Lh Ratio; Polycystic Ovary Syndrome; Ovarian Reserve; Assisted Reproduction*

Introduction

Subfertility affects roughly one in seven couples globally, creating intense social and clinical pressure in South Asian communities where delayed diagnostic workups are common [1,2]. In outpatient gynecology clinics and diagnostic laboratories across Punjab, Pakistan, basal serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) represent the first biochemical tests ordered when a woman fails to conceive after a year of unprotected intercourse [3]. Both glycoprotein hormones originate in anterior pituitary gonadotropes under hypothalamic gonadotropin-releasing hormone (GnRH) stimulation, yet they govern separate compartments of ovarian steroidogenesis. FSH promotes granulosa cell mitosis, aromatase activity, and early antral cohort recruitment during the luteal-follicular transition. LH acts primarily on theca interna cells to drive androgen precursor synthesis before triggering mid-cycle follicular rupture and corpus luteum maintenance [4].

Single-point hormone values often mislead. Pituitary LH discharges in rapid ultradian pulses every 60 to 90 minutes during the early follicular phase and clears from plasma within 20 minutes, whereas heavier sialylated FSH isoforms circulate for three to four hours [5]. A single venipuncture can easily catch a transient LH trough or surge. Functional derangements along the hypothalamic-pituitary-ovarian (HPO) axis also shift the relative proportion of FSH to LH long before either hormone breaches printed laboratory reference limits [6,7]. When the resting pool of primordial and pre-antral follicles begins to shrink, falling granulosa-cell inhibin B output weakens negative feedback on pituitary FSH synthesis without altering LH release [8]. The calculated serum FSH/LH ratio then climbs above 2.0 even while basal FSH stays below 10 mIU/mL [6,9].

An opposite neuroendocrine distortion characterizes chronic anovulation and polycystic ovary syndrome (PCOS). Rapid GnRH pulse frequency (>1 pulse per hour) selectively favors pituitary LH β-subunit gene transcription over FSH β-subunit transcription, while hyperinsulinemia and intra-ovarian androgen excess sensitize gonadotropes to GnRH [10,11]. Serum LH rises disproportionately relative to FSH, driving the FSH/LH ratio below 0.50 (or its reciprocal, the LH/FSH ratio, to 2.0 or higher) in a large fraction of anovulatory women [12]. Because regional diagnostic laboratories in Pakistan test young women with hyperandrogenic anovulation alongside older or prematurely aging women with follicular depletion, understanding how the FSH/LH ratio distributes across age groups is practically important. Anti-Müllerian hormone (AMH) assays and transvaginal antral follicle counts (AFC) offer sensitive ovarian reserve assessment [13], but high test prices limit their use during initial primary-care screening. Calculating the FSH/LH ratio from routine gonadotropin panels costs nothing extra. Here we analyze serum LH, FSH, and the FSH/LH ratio across 80 women presenting with infertility in Okara, examining non-parametric distributions, age-stratified trajectories, and diagnostic reclassification across normal and borderline basal FSH ranges.

Materials and Methods

Study Design and Patient Cohort

We conducted a cross-sectional analytical study at the Department of Allied Health Sciences (Medical Laboratory Technology), University of Okara, Okara, Pakistan, evaluating 80 women referred for laboratory investigation of primary or secondary infertility. Clinical infertility was defined per World Health Organization criteria as failure to achieve pregnancy after 12 months or more of regular unprotected intercourse. Women aged 17 to 48 years with complete serum gonadotropin records were eligible. We excluded patients who had taken exogenous gonadal steroids, clomiphene citrate, letrozole, or oral contraceptives within the preceding eight weeks, as well as women with prior oophorectomy, uncorrected thyroid disease, or hyperprolactinemia. All

patient records were assigned sequential alphanumeric codes (P01–P80) to protect confidentiality in accordance with institutional ethics guidelines and the Declaration of Helsinki.

Blood Sampling and Immunoassay Procedure

Venous blood (5.0 mL) was drawn from the antecubital vein into plain gel-clot activator tubes between cycle days 2 and 4 in cycling women, or on a random clinic day in women with prolonged oligomenorrhea or secondary amenorrhea. After clotting for 20 minutes at ambient temperature, specimens were centrifuged at 3,000 rpm for 10 minutes to separate clear serum. Grossly hemolyzed or lipemic sera were rejected. Serum LH and FSH concentrations (reported in mIU/mL, standardized against WHO 2nd International Standard 80/552 for LH and 94/632 for FSH) were measured on an automated chemiluminescence immunoassay (CLIA) platform. Technician batches included two-level commercial quality control sera; intra-assay and inter-assay coefficients of variation remained below 5.2% and 6.8%, respectively.

Endocrine Stratification and Statistical Analysis

For every patient, the serum FSH/LH ratio was calculated by dividing serum FSH by serum LH, and the reciprocal LH/FSH ratio was computed concurrently. Participants were grouped into three chronological age brackets reflecting reproductive stages: Group I (≤24 years, $n = 18$), Group II (25–34 years, $n = 39$), and Group III (≥35 years, $n = 23$). Based on published clinical thresholds [6,8,11,14], patients were also stratified into three gonadotropin ratio phenotypes: (1) LH-predominant (FSH/LH < 1.0, including the classic PCOS-associated biochemical cutoff of FSH/LH ≤ 0.50 or LH/FSH ≥ 2.0); (2) Concordant or balanced (FSH/LH 1.00–2.00); and (3) FSH-predominant diminished ovarian reserve (DOR) profile (FSH/LH > 2.00). Continuous data were summarized as both mean ± standard deviation (SD) and median with interquartile range (IQR). Because Shapiro–Wilk testing revealed severe departures from Gaussian normality across all hormonal metrics ($p < 0.001$), non-parametric tests were applied: Spearman's rank-order correlation (ρ) for bivariate relationships and the Kruskal–Wallis H test for multi-group age comparisons. Two-tailed p-values < 0.05 denoted statistical significance.

Results

Baseline Hormonal Distributions and Normality Testing

Eighty infertile women aged 17 to 48 years comprised the study population, with a mean age of 30.10 ± 7.00 years and a median age of 30.00 years (IQR 25.00–36.00 years; Table 1). Serum gonadotropin concentrations varied widely across individuals. Arithmetic mean concentrations were 16.21 ± 19.72 mIU/mL for LH (range 1.06–117.72 mIU/mL) and 17.08 ± 14.07 mIU/mL for FSH (range 1.92–65.86 mIU/mL). Because a subset of patients presented with severe hypergonadotropic ovarian failure or marked LH hypersecretion, parametric means were pulled well above the non-parametric medians of 10.16 mIU/mL for LH (IQR 5.45–18.37 mIU/mL) and 12.83 mIU/mL for FSH (IQR 7.36–21.81 mIU/mL). The serum FSH/LH ratio averaged 1.87 ± 2.13 overall, with a median of 1.50 (central IQR 1.00–2.17; Tukey hinge span 0.56–2.17) and extremes ranging from 0.14 to 13.64. Shapiro–Wilk testing confirmed that chronological age followed a normal distribution ($p = 0.184$), whereas serum LH, serum FSH, the FSH/LH ratio, and the reciprocal LH/FSH ratio were all strongly right-skewed ($p < 0.001$ for each; Table 1).

Table 1. Baseline Descriptive, Non-Parametric, and Normality Parameters of the Study Cohort (*N* = 80).

Variable	Mean ± SD	Median	IQR (Q1–Q3)	Min–Max	Shapiro–Wilk *p*
Chronological Age (years)	30.10 ± 7.00	30.00	25.00–36.00	17.00–48.00	0.184 (Normal)
Serum LH (mIU/mL)	16.21 ± 19.72	10.16	5.45–18.37	1.06–117.72	< 0.001*
Serum FSH (mIU/mL)	17.08 ± 14.07	12.83	7.36–21.81	1.92–65.86	< 0.001*
Serum FSH/LH Ratio	1.87 ± 2.13	1.50	1.00–2.17 (0.56–2.17)	0.14–13.64	< 0.001*
Reciprocal LH/FSH Ratio	1.22 ± 1.17	0.67	0.46–1.77	0.07–7.35	< 0.001*

*Note: SD = standard deviation; IQR = interquartile range; *Statistically significant departure from Gaussian normality (Shapiro–Wilk test, p < 0.001).*

Gonadotropin Profiles Across Maternal Age Strata

Stratifying the cohort by maternal age uncovered divergent hormonal trajectories between FSH and LH (Table 2). Nearly half of the women belonged to the 25–34-year age group (*n* = 39, 48.8%), with 18 patients (22.5%) aged ≤24 years and 23 patients (28.8%) aged ≥35 years. Serum FSH rose significantly across the three age brackets (Kruskal–Wallis $H = 6.530$, $p = 0.038$; Figure 2A). Median FSH increased from 9.93 mIU/mL in women aged ≤24 years and 10.50 mIU/mL in women aged 25–34 years to 15.99 mIU/mL (mean 23.25 ± 17.34 mIU/mL) in women aged ≥35 years. The proportion of women with elevated basal FSH (>10.0 mIU/mL) climbed steadily from 44.4% (8/18) in Group I and 56.4% (22/39) in Group II to 82.6% (19/23) in Group III ($p = 0.031$). LH followed a different trajectory. Young women (≤24 years) recorded the highest mean serum LH (21.41 ± 27.95 mIU/mL; median 12.66 mIU/mL), reflecting frequent hyper-LH anovulation (e.g., patient P71, age 17, LH = 117.72 mIU/mL; patient P20, age 21, LH = 67.34 mIU/mL). Consequently, the mean FSH/LH ratio was lowest in women ≤24 years (1.15 ± 0.79; median 0.78), rose to 1.57 ± 1.24 (median 1.68) at ages 25–34, and reached 2.96 ± 3.36 (median 1.47; IQR 0.72–4.46) in women ≥35 years.

Table 2. Comparison of Serum Gonadotropins and Ratio Indices Across Maternal Age Strata (*N* = 80).

Endocrine Parameter	Group I: ≤24 yrs (*n* = 18, 22.5%)	Group II: 25–34 yrs (*n* = 39, 48.8%)	Group III: ≥35 yrs (*n* = 23, 28.8%)	Statistic	*p*-value
Age (years), Mean ± SD	21.00 ± 2.30	29.18 ± 2.72	38.78 ± 3.33	—	—
Serum LH (mIU/mL), Mean ± SD [Med]	21.41 ± 27.95 [12.66]	13.78 ± 17.75 [8.09]	16.24 ± 14.72 [14.73]	H = 4.431	0.109

Serum FSH (mIU/mL), Mean ± SD [Med]	16.98 ± 14.48 [9.93]	13.48 ± 10.37 [10.50]	23.25 ± 17.34 [15.99]	H = 6.530	0.038*
FSH/LH Ratio, Mean ± SD [Med]	1.15 ± 0.79 [0.78]	1.57 ± 1.24 [1.68]	2.96 ± 3.36 [1.47]	H = 2.339	0.311
Reciprocal LH/FSH, Mean ± SD [Med]	1.40 ± 0.99 [1.31]	1.29 ± 1.39 [0.60]	0.95 ± 0.83 [0.68]	H = 2.339	0.311
Basal FSH > 10.0 mIU/mL, *n* (%)	8 (44.4%)	22 (56.4%)	19 (82.6%)	χ^2 = 6.942	0.031*

*Note: Med = non-parametric median; H = Kruskal–Wallis statistic; *Statistically significant difference across maternal age strata at p < 0.05.*

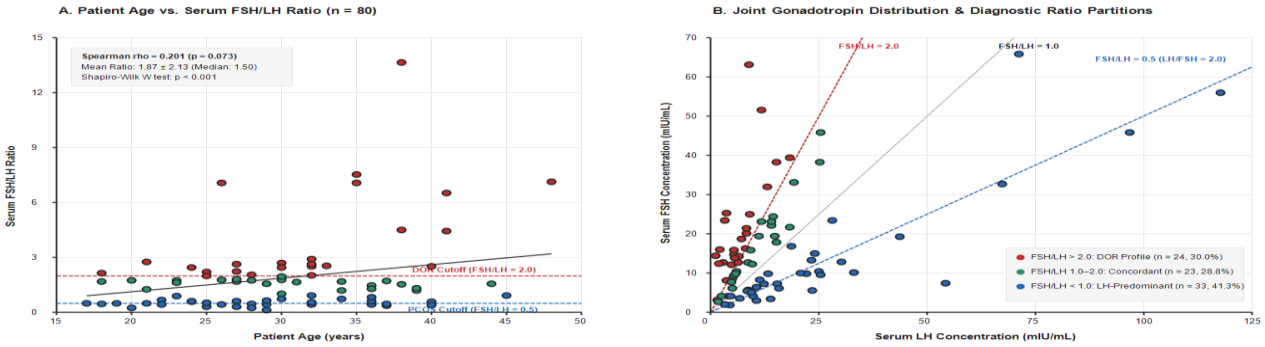

Figure 1. *(A) Scatterplot of maternal age against serum FSH/LH ratio (n = 80), illustrating the linear regression trend, Spearman rank correlation (ρ = 0.201, p = 0.073), and clinical cutoffs for diminished ovarian reserve (DOR, FSH/LH = 2.0) and PCOS (FSH/LH = 0.5). (B) Joint serum LH and FSH distribution partitioned by iso-ratio rays into DOR (red), concordant (teal), and LH-predominant (blue) zones.*

Bivariate Rank Correlations Among Age and Gonadotropins

Pairwise Spearman rank-order correlations are summarized in Table 3. Chronological age showed a weak positive rank correlation with the serum FSH/LH ratio (ρ = 0.201, t = 1.816, p = 0.073; Figure 1A) that remained slightly above the 0.05 significance threshold. Examining the two hormones separately clarified why: maternal age correlated positively and significantly with serum FSH (ρ = 0.234, t = 2.123, p = 0.037), whereas age had no correlation whatsoever with serum LH (ρ = 0.013, t = 0.118, p = 0.906). Serum FSH and LH were moderately and positively coupled (ρ = 0.398, p < 0.001), reflecting shared pituitary drive in women at the extremes of generalized hypergonadotropic ovarian failure (e.g., patient P74, age 45, LH = 71.16 mIU/mL, FSH = 65.86 mIU/mL) or hypogonadotropic hypogonadism (patient P65, age 27, LH = 3.31 mIU/mL, FSH = 1.99 mIU/mL). Across the cohort, the FSH/LH ratio was positively driven by FSH (ρ = 0.454, p < 0.001) and strongly suppressed by LH (ρ = −0.587, p < 0.001).

Table 3. Spearman Rank-Order Correlation Matrix (ρ) Among Age, Serum LH, Serum FSH, and Ratio Indices (*N* = 80).

Bivariate Parameter Pair	Spearman ρ	*t*-Statistic	Two-Tailed *p*	Physiological Interpretation
Age vs. Serum FSH/LH Ratio	+0.201	+1.816	0.073	Weak positive trend with maternal age
Age vs. Serum FSH Concentration	+0.234	+2.123	0.037*	Significant monotropic FSH elevation
Age vs. Serum LH Concentration	+0.013	+0.118	0.906	No monotonic age effect on basal LH
Serum FSH vs. Serum LH Concentration	+0.398	+3.831	< 0.001*	Coordinated pituitary gonadotropin release
FSH vs. Ratio | LH vs. Ratio	+0.454 | −0.587	+4.50 | −6.41	< 0.001*	Dual sensitivity to FSH and LH shifts

*Note: df = 78 for all pairwise rank correlations; *p < 0.05 statistically significant.*

Diagnostic Reclassification in Normal and Borderline Basal FSH Subgroups

Grouping patients by clinical FSH/LH cutoffs placed 33 women (41.3%) in the LH-predominant group (FSH/LH < 1.0), 23 women (28.8%) in the concordant group (1.00–2.00), and 24 women (30.0%) in the FSH-predominant DOR group (FSH/LH > 2.00; Table 4 and Figure 1B). Eighteen women (22.5% of the total cohort) met the classic PCOS biochemical threshold of LH/FSH ≥ 2.0 (FSH/LH ≤ 0.50). As shown in Figure 2B, LH predominance was most common in women ≤24 years (55.6%, 10/18) and declined to 38.5% (15/39) at ages 25–34 and 34.8% (8/23) at ages ≥35 years, whereas the DOR ratio phenotype (>2.0) doubled from 16.7% (3/18) in women ≤24 years to 33.3% (13/39) and 34.8% (8/23) in the older brackets. Normal basal FSH did not guarantee endocrine health. Thirty-one women (38.8%) had basal serum FSH ≤ 10.0 mIU/mL; within this ostensibly normal subgroup, ratio calculation unmasked a classic PCOS inversion (LH/FSH ≥ 2.0) in 11 women (35.5%; e.g., patient P17, age 29, FSH = 7.39 mIU/mL, LH = 54.29 mIU/mL, FSH/LH = 0.14; patient P59, age 28, FSH = 5.58 mIU/mL, LH = 23.47 mIU/mL, FSH/LH = 0.24) and an elevated DOR ratio (>2.0) in 2 women (6.5%; patient P18, age 28, FSH = 3.18 mIU/mL, LH = 1.55 mIU/mL, FSH/LH = 2.05). Among 15 patients with borderline basal FSH (10.1–15.0 mIU/mL), 8 women (53.3%) already exhibited an FSH/LH ratio > 2.0 (including patient P70, age 38, FSH = 14.46 mIU/mL, LH = 1.06 mIU/mL, FSH/LH = 13.64; and patient P21, age 38, FSH = 12.76 mIU/mL, LH = 2.84 mIU/mL, FSH/LH = 4.49), separating early ovarian reserve compromise from balanced gonadotropin output.

Table 4. Clinical Stratification of the Infertility Cohort by Serum FSH/LH Ratio Phenotypes (*N* = 80).

Gonadotropin Ratio Phenotype	Patients *n* (%)	Age (Years)	Serum LH [Median]	Serum FSH & Ratio [Med]
Phenotype 1: LH-Predominant (<1.0)	33 (41.3%)	28.79 ± 7.00	26.78 ± 26.70 [18.71]	FSH: 13.58 [8.27] | R: 0.53 [0.48]
• Classic PCOS Subgroup (LH/FSH ≥ 2.0)	18 (22.5%)	27.67 ± 6.84	34.72 ± 32.18 [23.33]	FSH: 13.65 [8.55] | R: 0.39 [0.43]

Phenotype 2: Concordant (1.00–2.00)	23 (28.8%)	30.43 ± 6.85	10.92 ± 6.76 [9.58]	FSH: 17.08 [15.89] | R: 1.56 [1.64]
Phenotype 3: DOR Profile (>2.00)	24 (30.0%)	31.58 ± 7.10	6.74 ± 4.39 [5.93]	FSH: 21.89 [16.14] | R: 4.03 [2.62]

Note: Values are Mean ± SD [Median]. DOR = diminished ovarian reserve; PCOS = polycystic ovary syndrome; R = FSH/LH ratio.

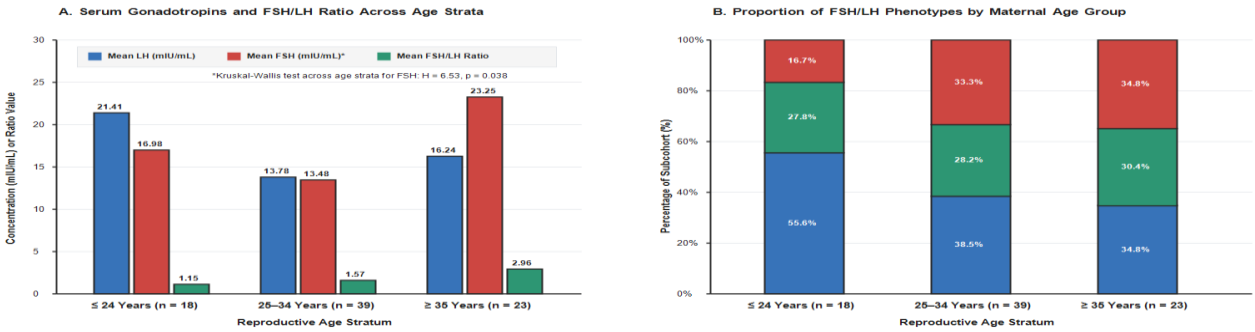

Figure 2. *(A) Arithmetic mean concentrations of serum LH, serum FSH, and the FSH/LH ratio across maternal age brackets (≤24, 25–34, and ≥35 years), showing the significant rise in FSH (Kruskal–Wallis H = 6.530, p = 0.038). (B) Stacked percentage distribution of LH-predominant (<1.0), concordant (1.0–2.0), and DOR (>2.0) ratio phenotypes by age group.*

Discussion

Interpreting basal gonadotropins in an unselected infertility clinic requires accounting for two biological processes that pull the FSH/LH ratio in opposite directions. In our 80-patient cohort from Okara, serum LH (16.21 ± 19.72 mIU/mL), serum FSH (17.08 ± 14.07 mIU/mL), and their ratio (1.87 ± 2.13; median 1.50; range 0.14–13.64) all deviated sharply from Gaussian normality (Shapiro–Wilk $p < 0.001$). Chronological age correlated significantly with absolute serum FSH ($\rho = 0.234$, $p = 0.037$) and produced a marked rise in median FSH across age brackets (from 9.93 mIU/mL at ≤24 years to 15.99 mIU/mL at ≥35 years; Kruskal–Wallis $p = 0.038$). Why, then, did the rank correlation between age and the composite FSH/LH ratio reach only $\rho = 0.201$ ($p = 0.073$)? Age alone did not explain the ratio because endocrine pathology in our clinic was bimodal. Young infertile women (≤24 years) clustered heavily in the low-ratio, hyper-LH zone (55.6% with FSH/LH < 1.0 and 33.3% with LH/FSH ≥ 2.0), whereas older women (≥35 years) shifted toward monotropic FSH elevation (mean ratio 2.96 ± 3.36). At the same time, premature ovarian depletion occurred in several women under 30 (such as patient P15, age 18, FSH = 39.37 mIU/mL, FSH/LH = 2.16; patient P42, age 21, FSH = 25.03 mIU/mL, FSH/LH = 2.76; and patient P27, age 26, FSH = 23.43 mIU/mL, FSH/LH = 7.06), while persistent hyper-LH anovulation appeared in women over 35 (e.g., patient P07, age 36, LH = 30.23 mIU/mL, FSH = 12.89 mIU/mL, FSH/LH = 0.43). This cross-age overlap blunted the simple linear slope between age and the FSH/LH ratio.

Our findings corroborate classic assisted reproduction studies demonstrating that an elevated day-3 FSH/LH ratio flags diminishing ovarian reserve before basal FSH crosses abnormal thresholds. Mukherjee et al. [6] and Barroso et al. [7] first reported that infertile women with day-3 FSH/LH ratios above 2.0 to 3.0—despite normal basal FSH (<10–12 mIU/mL)—suffered reduced peak estradiol responses, fewer retrieved oocytes, and higher cancellation rates during controlled ovarian hyperstimulation. Subsequent investigations by Shrim et al. [8], Seckin et al. [9], and Lyu

et al. [14] established the physiological mechanism: as the resting antral follicle cohort contracts, early follicular inhibin B falls [15], releasing pituitary FSH from negative feedback while basal LH remains low or slightly suppressed. In our cohort, the strong inverse correlation between LH and the FSH/LH ratio ($\rho = -0.587$, $p < 0.001$) alongside the positive correlation with FSH ($\rho = 0.454$, $p < 0.001$) mirrors the observations of Shrim et al. [8] and Prasad et al. [16]. Practically, among the 15 women in our sample whose basal FSH sat in the grey zone of 10.1–15.0 mIU/mL, more than half (8/15, 53.3%) already had an FSH/LH ratio > 2.0, immediately identifying patients who warrant expedited fertility counseling or modified gonadotropin dosing.

At the opposite end of the ratio scale, 41.3% of our cohort displayed an LH-predominant profile (FSH/LH < 1.0), and 22.5% met the classic PCOS cutoff of LH/FSH ≥ 2.0 (FSH/LH ≤ 0.50). Although the Rotterdam consensus criteria [12] do not mandate an elevated LH/FSH ratio to diagnose PCOS, regional endocrine studies from Pakistan and India show that gonadotropin inversion remains a hallmark of neuroendocrine PCOS phenotypes, especially in lean women and those with normal basal FSH [11,13,17]. In our dataset, 11 of the 31 women (35.5%) who had normal basal FSH (≤10.0 mIU/mL) exhibited an LH/FSH ratio ≥ 2.0. Cost matters in district laboratories. Where first-line AMH testing or high-resolution follicular sonography is financially out of reach for many patients [2,13], printing both the FSH/LH and LH/FSH ratios on standard immunoassay reports prevents clinicians from overlooking occult PCOS inversion or incipient ovarian reserve loss [18]. Limitations of this study include its single-center cross-sectional design ($N = 80$), single-venipuncture sampling subject to episodic LH pulsatility, and the absence of parallel AMH, estradiol, body mass index, and longitudinal pregnancy outcome records. Future prospective cohorts in Punjab should pair early-follicular FSH/LH ratios with AMH and antral follicle counts to establish population-specific receiver operating characteristic (ROC) cutoffs.

Conclusion

Serum LH, FSH, and the FSH/LH ratio follow strongly non-normal distributions ($p < 0.001$) in women presenting with infertility. While chronological age drives a statistically significant rise in serum FSH ($\rho = 0.234$, $p = 0.037$; Kruskal–Wallis $p = 0.038$), its correlation with the FSH/LH ratio remains weak ($\rho = 0.201$, $p = 0.073$) because hyper-LH ovulatory dysfunction in younger women and monotropic FSH elevation in older or prematurely aging women exert opposing pulls on the ratio. Categorizing patients by FSH/LH thresholds (<1.0, 1.00–2.00, and >2.00) partitions the infertility population into distinct neuroendocrine and ovarian-reserve phenotypes and unmasks actionable gonadotropin discordance in more than one-third of women whose isolated basal FSH appears normal or borderline. Routine calculation of both FSH/LH and LH/FSH ratios on clinical laboratory reports is a zero-cost practice that strengthens diagnostic workups in reproductive medicine.

Declarations: *Ethical Approval:* Approved by the Departmental Research Ethics Committee, Department of Allied Health Sciences, University of Okara; all patient data were anonymized prior to analysis. *Conflict of Interest:* None declared. *Funding:* None.

References

Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. *PLoS Med.* 2012;9(12):e1001356.

Tahir F, Majid S, Subhan F, Sultan S, Qayyum M. Causes of female infertility in Pakistan: a hospital-based clinico-epidemiological review. *Pak J Med Res.* 2014;53(2):38–42.

Practice Committee of the American Society for Reproductive Medicine. Testing and interpreting measures of ovarian reserve: a committee opinion. *Fertil Steril.* 2020;114(6):1151–1157.

Stamatiades GA, Kaiser UB. Gonadotropin regulation by pulsatile GnRH: signaling and gene expression. *Mol Cell Endocrinol.* 2018;463:131–141.

Filicori M, Santoro N, Merriam GR, Crowley WF Jr. Characterization of the physiological pattern of episodic gonadotropin secretion throughout the human menstrual cycle. *J Clin Endocrinol Metab.* 1986;62(6):1136–1144.

Mukherjee T, Copperman AB, Lapinski R, Sandler B, Bustillo M, Grunfeld L. An elevated day three follicle-stimulating hormone:luteinizing hormone ratio (FSH:LH) in the presence of a normal day 3 FSH predicts a poor response to controlled ovarian hyperstimulation. *Fertil Steril.* 1996;65(3):588–593.

Barroso G, Oehninger S, Monzo A, Kolm P, Gibbons WE, Muasher SJ. High FSH:LH ratio and low ovarian reserve: clinical value in assisted reproduction cycles. *J Assist Reprod Genet.* 2001;18(9):499–505.

Shrim A, Elizur SE, Seidman DS, Rabinovici J, Wiser A, Dor J. Elevated day 3 FSH/LH ratio due to low LH concentrations predicts reduced ovarian reserve. *Reprod Biomed Online.* 2006;12(4):418–422.

Seckin B, Turkcapar F, Ozaksit G. Elevated day 3 FSH/LH ratio: a marker to predict poor ovarian response in IVF/ICSI cycles. *J Assist Reprod Genet.* 2012;29(3):261–266.

McCartney CR, Eagleson CA, Marshall JC. Regulation of gonadotropin secretion: implications for polycystic ovary syndrome. *Semin Reprod Med.* 2002;20(4):317–326.

Banaszewska B, Spaczynski RZ, Pelesz M, Pawelczyk L. Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo- and hyperinsulinemia. *Rocz Akad Med Bialymst.* 2003;48:131–134.

Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril.* 2004;81(1):19–25.

Rehman R, Tariq S, Usmani A, Baig M. Interplay of follicle stimulating hormone, luteinizing hormone and anti-Müllerian hormone in infertile females of Karachi, Pakistan. *J Pak Med Assoc.* 2018;68(11):1635–1639.

Lyu SW, Kim JW, Choi CH, Seok HH, Yoon TK, Kim A. Impact of high basal FSH/LH ratio in women with normal FSH levels on in vitro fertilization outcomes. *Gynecol Endocrinol.* 2013;29(5):424–429.

Klein NA, Illingworth PJ, Groome NP, McNeilly AS, Battaglia DE, Soules MR. Decreased inhibin B secretion is associated with the monotropic FSH rise in older, ovulatory women: a study of serum and follicular fluid levels of dimeric inhibin A and B in spontaneous menstrual cycles. *J Clin Endocrinol Metab.* 1996;81(7):2742–2745.

Prasad S, Gupta T, Divya A. Correlation of the day 3 FSH/LH ratio and LH concentration in predicting outcome of controlled ovarian hyperstimulation and intrauterine insemination. *J Reprod Infertil.* 2013;14(3):133–138.

Malini NA, Roy George K. Evaluation of different ranges of LH:FSH ratios in polycystic ovarian syndrome (PCOS) – Clinical based case control study. *Gen Comp Endocrinol.* 2018;260:51–57.

Ho HY, Lee RK, Lin MH, Hwu YM. Estradiol and FSH/LH ratio as predictors of ovarian response to gonadotropin stimulation in patients with normal basal FSH levels. *Taiwan J Obstet Gynecol.* 2005;44(3):250–255.