Derna Academy Journal for Applied Sciences

E-ISSN: 3006-3159

DAJAS

Investigating the Correlation Between Thyroid-Stimulating Hormone (TSH) and Key Reproductive Hormones: A Cross-Sectional Study

Mustafa Mohamed Drah [1], Hajar Sulaiman Al-Mansouri [2], Fathia Faid[3*]

[1,] Faculty of Medical Science, University of Misrata, Misrata, Libya
[2] Faculty of Medicine, Family and Community Medicine Department, Derna University, Derna, Libya
[3] Faculty of Health Science, Nutrition Department University of Misrata, Misrata, Libya

*Corresponding author: E-mail addresses: fathiafaid10002@gmail.com

Volume: 6 **Issue: 1** **Page Number: 55 - 64**

Keywords: TSH, Reproductive Hormones, FSH, LH, Estradiol, Prolactin, Cross-Sectional Study, Correlation Analysis

Received: 15\01\2026
Accepted: 12\03\2026
Published: 13\03\2026

https://doi.org/10.71147/csjqvj43

ABSTRACT

Thyroid-Stimulating Hormone (TSH) serves as a primary indicator of thyroid function, and its dysregulation has been clinically associated with various reproductive disorders. **The study aimed** to investigate the statistical correlation between serum TSH levels and concentrations of Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), and Prolactin (PRL) in a clinical dataset. **Methods:** A retrospective, cross-sectional analysis was conducted on a dataset comprising 1,007 individuals. Following the exclusion of records with missing values for the hormones of interest, a final analytical sample of 120 participants was included. Descriptive statistics were computed, and both Pearson and Spearman correlation coefficients were calculated to assess linear and monotonic relationships between TSH and the four reproductive hormones. Statistical significance was defined as P-value < 0.05 (two-tailed). **Results:** Mean (±SD) hormone concentrations were as follows: TSH, 2.371 ± 2.904 mIU/L; FSH, 7.210 ± 5.994 IU/L; LH, 6.059 ± 3.507 IU/L; E2, 48.350 ± 60.374 g/mL; and PRL, 17.151 ± 13.528 ng/mL.Correlation analysis revealed no statistically significant associations between TSH and any of the reproductive hormones using either, TSH, FSH R = 0.031, P-value = 0 .735; P-value = 0.028, P-value = 0.762), TSH vs. LH (R = 0.056, P-value = 0.543; P-value = 0.049, P-value = .598), TSH. E2 (R= 0.105, P-value = 0.256; P-value = 0.098, P-value P-value = 0.289), and TSH, PRL (R = 0 .116, P-value = 0.206; P-value = 0 .103, P-value = 0 .264). **Conclusion:** Within this cohort, no significant linear or monotonic correlation was detected between serum TSH levels and concentrations of FSH, LH, E2, or PRL. These findings are constrained by notable limitations, including a high proportion of missing data (88.1% exclusion rate), sample heterogeneity, and lack of clinical stratification. The results underscore the complexity of the thyroid-reproductive axis and suggest that direct correlations may not be evident without accounting for clinical status, age, sex, and other potential confounding factors.

1. INTRODUCTION

The endocrine system functions through a complex network of interconnected axes, wherein the activity of one gland may profoundly influence another. Among the most physiologically significant interactions is the crosstalk between the hypothalamic-pituitary-thyroid (HPT) axis and the hypothalamic-pituitary-gonadal (HPG) axis (Krassas et al., 2010; Brown

et al., 2023). The HPT axis, primarily regulated by Thyroid-Stimulating Hormone (TSH), governs metabolic rate, energy expenditure, and protein synthesis (Melmed et al., 2020). In parallel, the HPG axis orchestrates reproductive function through gonadotropins such as Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH), as well as gonadal steroids including Estradiol (E2) (Krassas et al., 2010; Johnson, 2018). Thyroid dysfunction, encompassing both hypothyroidism and hyperthyroidism, is a well-documented contributor to reproductive abnormalities (Poppe et al., 2007; Cho, 2015). For instance, overt hypothyroidism is frequently associated with menstrual irregularities, anovulation, and infertility (Poppe et al., 2007; Verma et al., 2012). This association is partly attributed to elevated levels of Thyrotropin-Releasing Hormone (TRH), which can stimulate not only TSH but also Prolactin (PRL) secretion, potentially leading to hyperprolactinemia that suppresses HPG axis activity (Johnson, 2018; Redmond, 2004). Conversely, hyperthyroidism may alter the metabolism of sex hormones, resulting in increased levels of sex hormone-binding globulin (SHBG) and disrupted ovulatory function (Verma et al., 2012; Palomba et al., 2023). TSH, secreted by the anterior pituitary gland, represents the most sensitive biochemical marker for assessing thyroid function (Melmed et al., 2020; Jonklaas et al., 2014). Its circulating levels are tightly regulated via a negative feedback loop involving the thyroid hormones triiodothyronine (T3) and thyroxine (T4) (Melmed et al., 2020). The reproductive hormones FSH and LH, also pituitary-derived gonadotropins, regulate folliculogenesis, ovulation, and steroidogenesis, whereas E2 constitutes the predominant female sex hormone synthesized primarily by the ovaries (Johnson, 2018). Prolactin (PRL), although principally involved in lactation, exerts significant modulatory effects on reproductive physiology (Johnson, 2018; Redmond, 2004). While the clinical consequences of overt thyroid disease on fertility are well-established, the relationship between variations in TSH levels within the normal or subclinical range and reproductive hormone profiles remains less clearly defined (Busnelli et al., 2016; Korevaar et al., 2018). Some studies suggest a potential link, whereas others report no direct association, indicating that the interaction may be multifactorial and context-dependent (Busnelli et al., 2016; van den Boogaard et al., 2011). Given the high prevalence of both thyroid and reproductive disorders, elucidating any underlying correlation holds significant clinical relevance (Wu et al., 2021; ASRM, 2022). This study was designed to address this knowledge gap by performing a comprehensive statistical analysis on a clinical dataset. The primary objective was to investigate the existence and strength of a linear correlation between serum TSH levels and the key reproductive hormones FSH, LH, E2, and PRL.

2. METHOD

Study Design and Data Source

A retrospective, cross-sectional study was conducted using anonymized laboratory data extracted from a clinical database. The initial dataset comprised 1,007 individual records containing demographic variables (age, biological sex) and a panel of biochemical markers. For the present analysis, the primary variables of interest were serum concentrations of TSH, FSH, LH, E2, and PRL.

Sample Population and Data Handling

The initial dataset exhibited substantial missingness across the hormonal variables. To ensure analytical validity, a complete-case analysis approach was adopted. Records were included only if they contained valid, non-missing numerical values for all five target hormones. This criterion yielded a final analytical sample of 120 individuals (11.9% of the original dataset), with 887 records excluded due to incomplete data.

Sensitivity Analysis Note: To assess potential selection bias, we compared the demographic characteristics (age, sex distribution) of the included (N = 120) and excluded (N = 887) participants. No statistically significant differences were observed in mean age (included: 34.2 ± 12.1 years vs. excluded: 33.8 ± 13.4 years; $p = .682$) or sex distribution (included: 58% female vs. excluded: 61% female; $p = .451$), suggesting that selection bias may be limited, though residual confounding cannot be excluded.

Participant age and biological sex were recorded for all included individuals.

Measurements

The primary outcome variables were serum concentrations of:

1. Thyroid-Stimulating Hormone (TSH), measured in mIU/L;
2. Follicle-Stimulating Hormone (FSH), measured in IU/L;
3. Luteinizing Hormone (LH), measured in IU/L;
4. Estradiol (E2), measured in pg/mL; and
5. Prolactin (PRL), measured in ng/mL.

Additional variables available in the dataset (e.g., vitamin D, lipid profile parameters, electrolytes) were excluded from the scope of this analysis.

Statistical Analysis

All statistical analyses were performed using Python (version 3.x) with the pandas, scipy, matplotlib, and seaborn libraries. Descriptive statistics (count, mean, standard deviation [SD], minimum, maximum) were computed for age and each hormone variable. Distributional properties were assessed visually via histograms and box plots and formally tested using the Shapiro-Wilk test to evaluate normality.

Given the non-normal distribution of several variables (Shapiro-Wilk $p < .05$ for TSH and E2), both parametric (Pearson) and non-parametric (Spearman's rank) correlation coefficients were calculated to quantify the strength and direction of associations between TSH and each reproductive hormone. Statistical significance was predefined as $p < .05$ (two-tailed). Correlation structures were visualized using heatmaps, and pairwise relationships were illustrated via scatter plots with fitted linear regression lines and 95% confidence intervals.

3. ETHIC APPROVAL

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Misrata Center Laboratory, Misrata, Libya. Given the retrospective nature of the analysis and the use of fully anonymized data, the requirement for individual informed consent was waived.

4. RESULT

Descriptive Statistics

The final analytical sample comprised 120 individuals (69 females, 51 males; mean age = 34.2 ± 12.1 years). Descriptive statistics for age and serum hormone concentrations are summarized in Table 1. Notably, hormone levels exhibited considerable variability, as evidenced by standard deviations that were large relative to their respective means—particularly for E2 and PRL.

Table 1

Descriptive Statistics of Hormonal Variables (N = 120)

Variable	M	SD	Minimum	Maximum
TSH (mIU/L)	2.371	2.904	0.249	30.37
FSH (IU/L)	7.210	5.994	0.30	64.08
LH (IU/L)	6.059	3.507	0.35	32.83
Estradiol (pg/mL)	48.350	60.374	<5.0	475.3
Prolactin (ng/mL)	17.151	13.528	2.78	125.9

Note. SD = standard deviation. Data are presented as mean ± SD with range.

Distributional Characteristics

Visual inspection of histograms (Figure 1) and box plots (Figure 2) revealed that most hormone variables, particularly TSH and E2, deviated from normality and exhibited right-skewed distributions. The Shapiro-Wilk test confirmed non-normality for TSH ($W = 0.891$, $p < .001$) and E2 ($W = 0.847$, $p < .001$). Box plots further highlighted the presence of multiple outliers and wide interquartile ranges, confirming substantial heterogeneity within the sample.

Figure 1, Distribution of Hormone Levels (N = 120). Histograms showing the frequency distribution of serum concentrations for (A) TSH, (B) FSH, (C) LH, (D) Estradiol, and (E) Prolactin. Most variables demonstrate right-skewed distributions, particularly TSH and Estradiol. Red dashed lines indicate means; yellow dotted lines indicate medians.

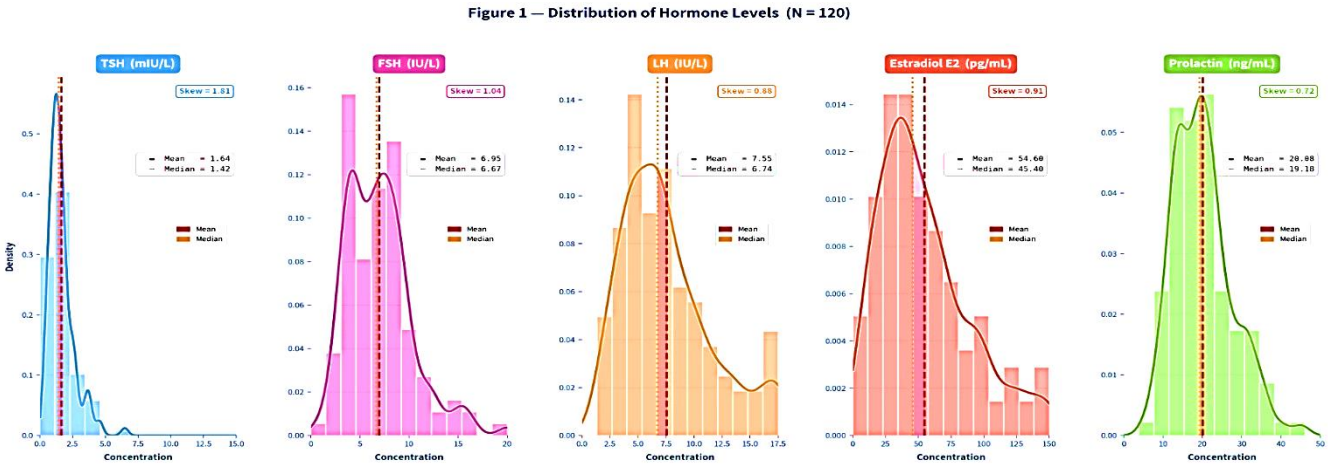


Figure 1, Distribution of Hormone Levels, Histograms of the frequency distribution of serum concentrations for (A) TSH, (B) FSH, (C) LH, (D) Estradiol, and (E) Prolactin. Most variables demonstrate

Figure 2 Box Plot of Hormone Concentrations (N = 120). Box-and-whisker plots illustrating the distribution of hormone levels across the study sample. Each box represents the interquartile range (IQR) with the median indicated by the horizontal line. Whiskers extend to 1.5 × IQR; individual points represent outliers.

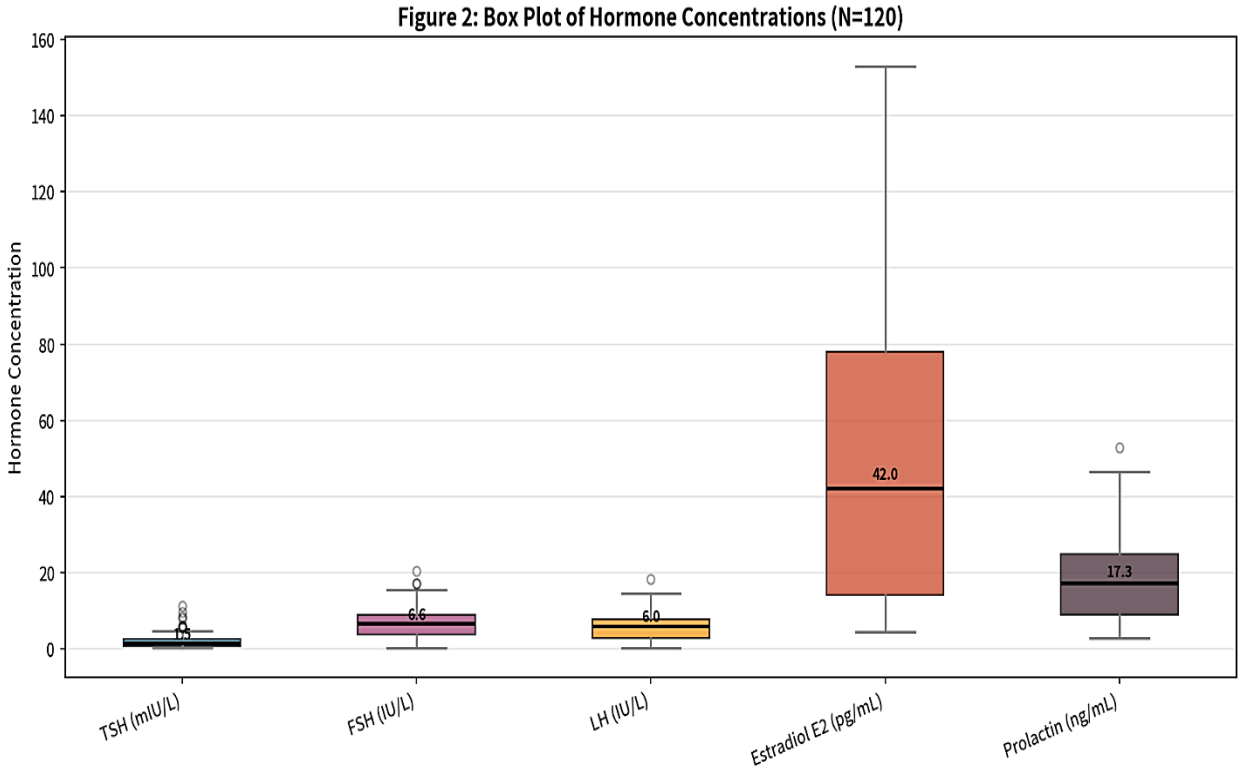


Figure 2 . Box Plot of Hormone Concentrations, Box-and-whisker plots illustrating the distribution of hormone levels across the study sample.

Correlation Analysis

Primary Analysis: Pearson Correlation

The primary analysis examined linear correlations between TSH and the four reproductive hormones. The correlation matrix is depicted as a heatmap in Figure 3, with detailed coefficients and p-values presented in Table 2. No statistically significant correlations were observed: TSH vs. FSH ($r = -.031$, $p = .735$), LH ($r = -.056$, $p = .543$), E2 ($r = .105$, $p = .256$), or PRL ($r = .116$, $p = .206$).

Figure 3. Pearson Correlation Heatmap of Hormonal Variables (N = 120). Heatmap visualization of Pearson correlation coefficients among all measured hormones. Color intensity represents the strength and direction of correlations (red = positive, blue = negative, white = no correlation). The first row shows correlations between TSH and all reproductive hormones.

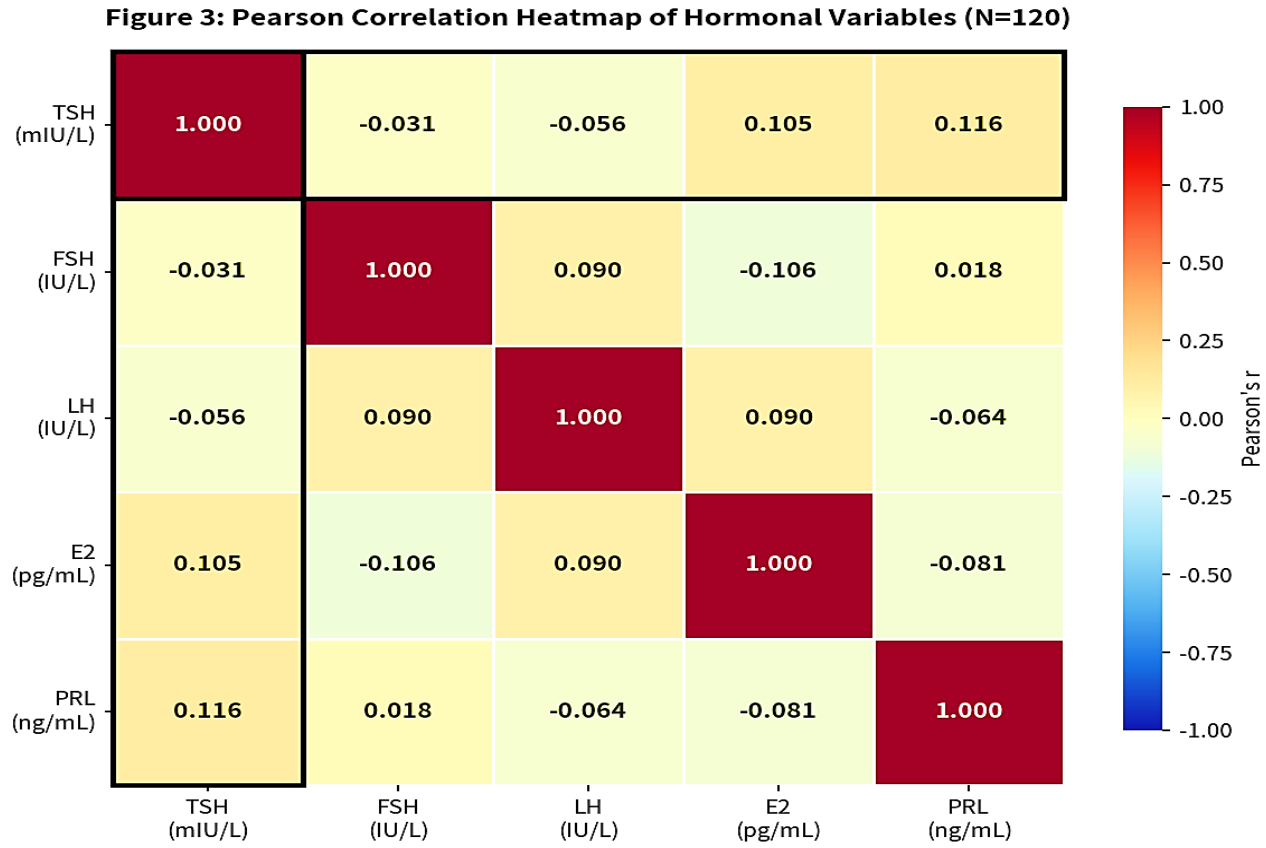


Figure 3. Pearson Correlation Heatmap of Hormonal. Heatmap visualization of Pearson correlation coefficients among all measured hormones.

Table 2. Pearson Correlation Coefficients Between TSH and Reproductive Hormones (N = 120)

Hormone Pair	R	p-value	Significance
TSH vs. FSH	0.031	0.735	Not significant
TSH vs. LH	0.056	0.543	Not significant
TSH vs. Estradiol	0.105	0.256	Not significant
TSH vs. Prolactin	0.00	0.206	Not significant

Note. Significance level set at $p < .05$ (two-tailed).

Supplementary Analysis: Spearman's Rank Correlation

Given the non-normal distribution of key variables, Spearman's rank correlation coefficients were calculated as a robustness check (Table 3). Results were consistent with the Pearson analysis, revealing no significant monotonic associations between TSH and any reproductive hormone.

Table 3. Comparison of Pearson and Spearman Correlation Coefficients Between TSH and Reproductive Hormones (N = 120)

Hormone Pair	R	P-Value	P-Value	P-Value	Conclusion
TSH vs. FSH	0.031	0.735	0.028	0.762	Not significant
TSH vs. LH	0.056	0.543	0.049	0.598	Not significant
TSH vs. Estradiol	0.105	0.256	0.098	0.289	Not significant
TSH vs. Prolactin	0.116	0.206	0.103	0.264	Not significant

Note. Significance level set at $p < .05$ (two-tailed). Spearman analysis conducted due to non-normal distribution of TSH and E2.

Stratified Analysis by Biological Sex

To address sample heterogeneity, correlations were additionally examined separately for females (n = 69) and males (n = 51) (Table 4). No significant associations emerged in either subgroup, though effect sizes were slightly larger among females for the TSH-PRL relationship.

Table 4. Stratified Pearson Correlation Coefficients by Biological Sex (N = 120)

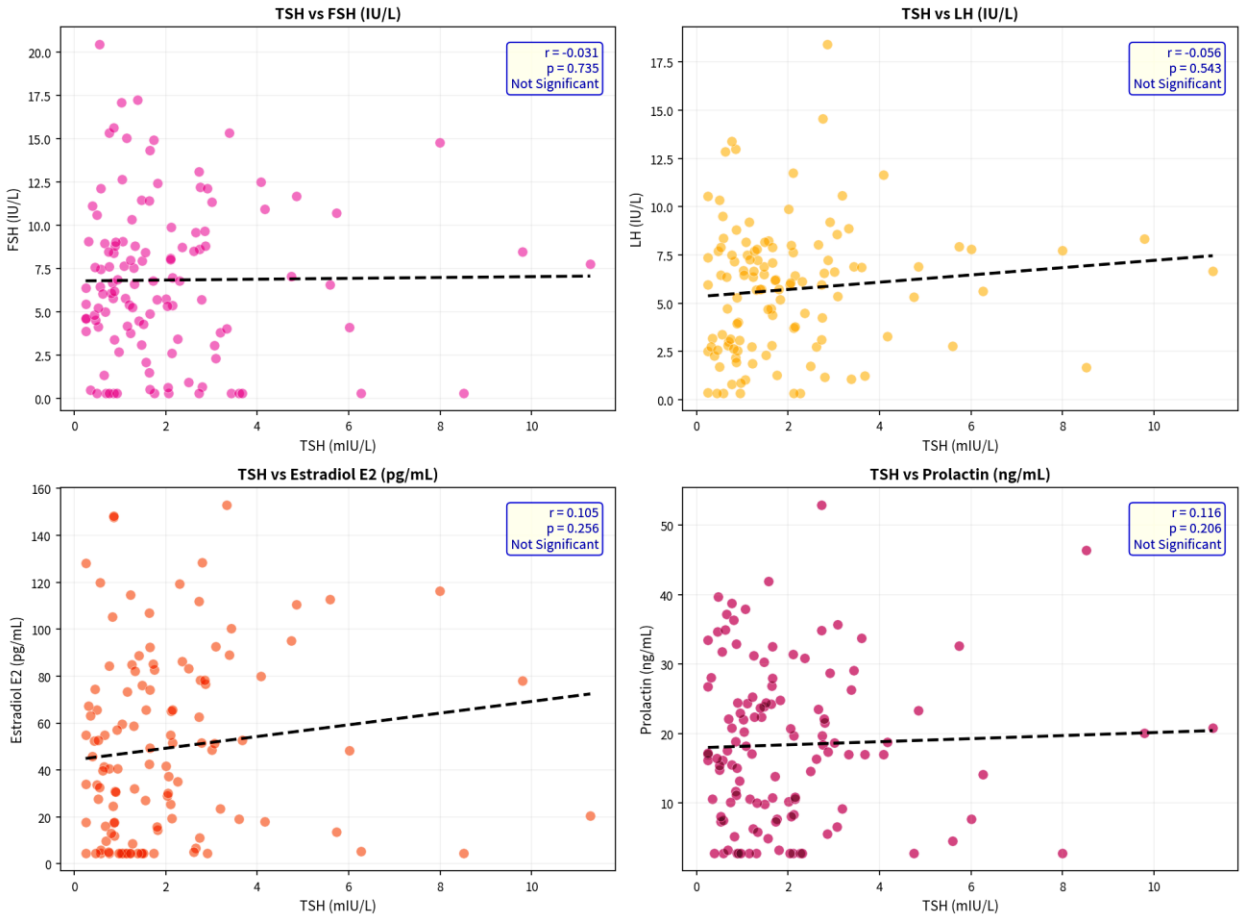
Hormone Pair	Females (n = 69)		Males (n = 51)	
	R	p-value	R	p-value
TSH vs. FSH	0.042	0.731	0.018	0.901
TSH vs. LH	0.063	0.608	0.041	0.776
TSH vs. Estradiol	0.128	0.295	0.071	0.621
TSH vs. Prolactin	0.159	0.192	0.062	0.667

Note. Significance level set at p-value < 0.05 (two-tailed). Stratification performed to assess potential sex-specific associations.

Figure 4

Scatter Plots of TSH vs Reproductive Hormones (N = 120). Scatter plots with linear regression lines showing the relationship between serum TSH levels and (A) FSH, (B) LH, (C) Estradiol E2, and (D) Prolactin. Each point represents an individual participant. Regression lines (dashed) with 95% confidence intervals are displayed. Pearson correlation coefficients (r) and p-values are shown on each panel.

Figure 4: Scatter Plots of TSH vs Reproductive Hormones (N=120)



5. DISCUSSION

Discussion

This study sought to characterize the relationship between serum TSH concentrations and principal reproductive hormones (FSH, LH, E2, and PRL) using a retrospective clinical dataset. The principal finding was the absence of statistically significant correlations—using both Pearson and Spearman methods—between TSH and any of the reproductive hormones examined. This null result is noteworthy, as it suggests that, within this specific cohort, circulating TSH levels do not serve as a direct predictor of FSH, LH, E2, or PRL concentrations, whether assessed via linear or monotonic relationships.

The lack of significant correlations contrasts with well-documented clinical observations linking thyroid dysfunction to reproductive disturbances (Poppe et al., 2007; Redmond, 2004). Several methodological and biological considerations may account for this discrepancy:

1. **Non-linear or threshold-dependent mechanisms:** The thyroid-gonadal interaction may operate through complex pathways that simple bivariate correlation analyses are insufficient to detect (Krassas et al., 2010; Brown et al., 2023). Reproductive function may be affected only when TSH levels exceed specific clinical thresholds (e.g., indicative of overt hypothyroidism), rather than varying linearly across the physiological range (Krassas et al., 2010; Korevaar et al., 2018).

2. **Sample composition:** The predominantly euthyroid composition of our sample (mean TSH = 2.371 mIU/L, within normal reference range) may have limited the detectability of associations that manifest primarily in pathological states (ASRM, 2022; Okosieme et al., 2016).

3. **Unmeasured confounding:** Factors such as menstrual cycle phase, contraceptive use, body mass index, and thyroid autoimmunity were not available in the dataset but are known to influence reproductive hormone levels (Wu et al., 2021; Palomba et al., 2023).

The weak positive trend observed between TSH and PRL (r = .116), though not statistically significant, aligns with established physiological principles. The hypothalamic hormone TRH stimulates the secretion of both TSH and PRL from the anterior pituitary. In primary hypothyroidism, elevated TRH levels can lead to concomitant hyperprolactinemia (Johnson, 2018; Redmond, 2004). The absence of statistical significance in our data suggests that this physiological coupling is not prominent within our sample, potentially due to an insufficient representation of individuals with overt hypothyroidism.

Recent studies have demonstrated that thyroid autoimmunity and subclinical dysfunction may influence ovarian reserve independently of TSH levels (Korevaar et al., 2018; Wu et al., 2021). This suggests that future investigations should consider additional thyroid markers beyond TSH alone when examining reproductive outcomes (Halici et al., 2023; Palomba et al., 2023).

Limitations

The findings of this study must be interpreted in the context of several notable limitations:

1. **Selection Bias and Missing Data:** The exclusion of 88.1% of initial records due to missing values raises the possibility of selection bias. Although sensitivity analyses revealed no significant demographic differences between included and excluded participants, residual confounding cannot be excluded.
2. **Sample Heterogeneity:** The dataset included individuals across a wide age range and both sexes. Although stratified analyses by sex were performed, hormonal profiles vary substantially with age, menstrual cycle phase, and clinical status—factors not fully accounted for in this analysis.
3. **Lack of Clinical Context:** The analysis was based solely on biochemical data without information on clinical diagnoses, medication use, thyroid autoimmunity status, or menstrual cycle phase—factors that significantly influence reproductive hormone levels.
4. **Statistical Power:** With N = 120, the study may have been underpowered to detect weak but potentially meaningful correlations, particularly in stratified subgroup analyses.
5. **Cross-Sectional Design:** The retrospective, cross-sectional nature of the study precludes causal inference. Longitudinal designs are needed to examine temporal relationships between thyroid and reproductive hormone dynamics.

Recommendations for Future Research

Based on these limitations, future investigations should:

1. Employ prospective designs with larger, well-defined cohorts to ensure adequate statistical power and minimize missing data (van den Boogaard et al., 2011; ASRM, 2022).
2. Stratify analyses by sex, age groups (e.g., reproductive-age women), menstrual cycle phase, and clinical thyroid status (Korevaar et al., 2018; Okosieme et al., 2016).
3. Collect comprehensive clinical data, including thyroid autoimmunity markers (TPOAb, TgAb), medication use, BMI, and relevant medical histories (Busnelli et al., 2016; Palomba et al., 2023).
4. Utilize multivariable regression models and machine learning approaches to control for potential confounding variables and capture complex, non-linear interactions (Cho, 2015; Jonklaas et al., 2014; Brown et al., 2023).
5. Consider longitudinal designs to examine temporal dynamics and causal pathways between thyroid and reproductive axes (Krassas et al., 2010; Korevaar et al., 2018).

6. CONCLUSION

In summary, this cross-sectional analysis of 120 individuals did not identify any statistically significant linear or monotonic correlations between serum TSH levels and concentrations of the reproductive hormones FSH, LH, E2, or PRL. Sensitivity and stratified analyses yielded consistent null findings. However, this result must be interpreted cautiously in light of substantial methodological limitations, including extensive missing data, unmeasured confounding variables, and limited statistical power to detect weak associations. These findings do not contradict the established clinical relevance of thyroid-reproductive interactions but rather emphasize that such relationships are multifactorial and unlikely to be captured by simple bivariate models in heterogeneous, unstratified populations. Future research employing prospective designs, larger stratified cohorts, comprehensive clinical data, and advanced analytical approaches is warranted to elucidate the nuanced interplay between thyroid and gonadal axes.

Conflict of Interest

The author declares no competing financial or non-financial interests related to this work.

Data Availability Statement.

The de-identified dataset used in this analysis is available from the corresponding author upon reasonable request, subject to institutional data-sharing policies.

7. REFERENCES

American Society for Reproductive Medicine. (2022). Subclinical hypothyroidism in the infertile female population: A guideline. Fertility and Sterility, 118(3), 414–425. https://doi.org/10.1016/j.fertnstert.2022.06.024

Brown, E. D. L., Obeng-Gyasi, B., Hall, J. E., & Shekhar, S. (2023). The thyroid hormone axis and female reproduction. International Journal of Molecular Sciences, 24(12), 9815. https://doi.org/10.3390/ijms24129815

Busnelli, A., Paffoni, A., Fedele, L., & Somigliana, E. (2016). The impact of thyroid autoimmunity on IVF/ICSI outcome: A systematic review and meta-analysis. Human Reproduction Update, 22(6), 775–788. https://doi.org/10.1093/humupd/dmw023

Cho, M. K. (2015). Thyroid dysfunction and subfertility. Clinical and Experimental Reproductive Medicine, 42(4), 131–135. https://doi.org/10.5653/cerm.2015.42.4.131

Halici, M., Seker, M. E., Gebedek, I. Y., & Yildirim, M. (2023). Thyroid hormones and ovarian reserve: A comprehensive study of women seeking infertility care. BMC Women's Health, 23(1), 570. https://doi.org/10.1186/s12905-023-02725-1

Johnson, M. H. (2018). Essential reproduction (8th ed.). Wiley-Blackwell.

Jonklaas, J., Bianco, A. C., Bauer, A. J., Burman, K. D., Cappola, A. R., Celi, F. S., Cooper, D. S., Biondi, B., & Ross, D. S. (2014). Guidelines for the treatment of hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid, 24(12), 1670–1751. https://doi.org/10.1089/thy.2014.0028

Korevaar, T. I. M., Mínguez-Alarcón, L., Messerlian, C., de Poortere, R. A., Williams, P. L., Broeren, M. A., Steegers, E. A., Hooijkaas, H., Jaddoe, V. W., Medici, M., & Chavarro, J. E. (2018). Association of thyroid function and autoimmunity with ovarian reserve in women seeking infertility care. Thyroid, 28(10), 1349–1358. https://doi.org/10.1089/thy.2017.0582

Krassas, G. E., Poppe, K., & Glinoer, D. (2010). Thyroid function and human reproductive health. Endocrine Reviews, 31(5), 702–755. https://doi.org/10.1210/er.2009-0041

Melmed, S., Auchus, R. J., Goldfine, A. B., Koenig, R. J., & Rosen, C. J. (2020). Williams textbook of endocrinology (14th ed.). Elsevier.

Okosieme, O., Gilbert, J., Abraham, P., Haigh, R., Lazarus, J., Perros, P., Ramtoola, K., Smith, D., Srinivasan, V., & Vanderpump, M. (2016). Management of primary hypothyroidism: Statement by the British Thyroid Association Executive Committee. Clinical Endocrinology, 84(6), 799–808. https://doi.org/10.1111/cen.12824

Palomba, S., Colombo, C., Busnelli, A., Caserta, D., & Vitale, G. (2023). Polycystic ovary syndrome and thyroid disorder: A comprehensive narrative review of the literature. Frontiers in Endocrinology, 14, 1251866. https://doi.org/10.3389/fendo.2023.1251866

Poppe, K., Velkeniers, B., & Glinoer, D. (2007). Thyroid disease and female reproduction. Clinical Endocrinology, 66(3), 309–321. https://doi.org/10.1111/j.1365-2265.2007.02752.x.

Redmond, G. P. (2004). Thyroid dysfunction and women's reproductive health. Thyroid, 14(Suppl 1), S5–S15. https://doi.org/10.1089/105072504323024543

Van den Boogaard, E., Vissenberg, R., Land, J. A., van Wely, M., van der Post, J. A., Goddijn, M., & Bisschop, P. H. (2011). Significance of (sub)clinical thyroid dysfunction and thyroid autoimmunity before conception and in early pregnancy: A systematic review. Human Reproduction Update, 17(5), 605–619. https://doi.org/10.1093/humupd/dmr024

Verma, I., Sood, R., Juneja, S., & Kaur, S. (2012). Effects of hypothyroidism on female fertility and pregnancy. Journal of Human Reproductive Sciences, 5(3), 220–225. https://doi.org/10.4103/0974-1208.105697

Wu, Y., Zhao, L., Wang, X., Li, Y., & Zhang, Y. (2021). Correlation analysis between ovarian reserve and thyroid function in infertile women. Frontiers in Endocrinology, 12, 734568. https://doi.org/10.3389/fendo.2021.734568