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Research Article

Hormonal Regulation of Female Adipose Regionality: A Framework for Precision Drug Targeting

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Received Date: 02 July 2025 | Accepted Date: 14 July 2025 | Published Date: 28 July 2025

Citation: Rehan Haider, Hina Abbas, Shabana Naz Shah, (2025), Hormonal Regulation of Female Adipose Regionality: A Framework for Precision Drug Targeting, *Clinical Genetic Research*, 4(4); **Doi:**10.31579/2834-8532/057

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Abstract

The phenotype of regional adiposity in women, especially in breast and gluteofemoral regions, is increasingly recognized as a hormone-regulated phenotype that may be relevant for precision pharmacotherapy. In addition to the widely acknowledged influence of estrogen, progesterone, and androgens on fat distribution, emerging evidence underlines complementary roles of leptin, adiponectin, and local aromatase activity in site-specific adipose tissue expansion. The aim of this study is to synthesize current hormonal, molecular, and pharmacological data into an integrated format that would propose a framework for drug targeting of female adipose regionality.

In the present study, a cross-sectional analysis was performed in 412 women aged 18–45 years, in whom circulating sex hormones, metabolic biomarkers, and body-composition parameters were measured by DXA and 3-D anthropometry. Estrogen-to-androgen ratio, leptin levels, and regional aromatase activity were identified as the top predictors of breast and gluteal adiposity in multivariate regression and partial-least-squares modeling ($p < 0.001$). Gluteofemoral fat showed more robust associations with estrogen signaling and adiponectin than did central adiposity, whereas breast adiposity was more sensitive to progesterone and local aromatase expression.

These findings support the development of targeted therapeutics aimed at modulating regional fat distribution for metabolic, endocrine, and aesthetic applications. In this regard, a framework is proposed that integrates knowledge on endocrine pathways, receptor distribution, and adipocyte site-specific biology to guide precision drug design. Furthermore, hormonal profiling can also enable patient stratification for future clinical trials of lipomodulating agents.

Overall, this study furthers the understanding of hormone-driven adipose regionality and sets biologically founded targets for the next generation of pharmacological interventions.

Keywords: female adiposity; regional fat distribution; estrogen; aromatase; leptin; precision pharmacology; breast adiposity; gluteofemoral fat; endocrine regulation

Introduction

Female adipose regionality is the result of complex hormonal interactions among estrogen, progesterone, and androgens, with paracrine activity within adipose depots supporting these processes (1–4). Breast and gluteofemoral adiposity possess different metabolic profiles and confer differential cardiometabolic risk factors (5). Understanding endocrine influences on these regions is important to inform novel pharmaceutical strategies aimed at selective modulation of fat.

Literature Review

This section summarizes the current understanding of hormonal influences on regional adiposity and highlights increasing pharmaceutical interest in this area.

Statistical Analysis

- Normality tested using Shapiro–Wilk.
- Group differences analyzed by ANOVA.
- Multivariate regression examining hormone–region relationships.
- PLS-path modeling for endocrine → adiposity pathways.
- Significance level $p < 0.05$.

Research Methodology

Design: Cross-sectional observational.

Sample: 412 healthy women (18–45 years).

Measurements: DXA, 3-D body scan, serum estrogen, progesterone, testosterone, leptin, adiponectin, aromatase mRNA from peripheral fat biopsy.

Tools: ELISA, qPCR, multivariate analytics.

Results

(Text-Only Summary)

• Estrogen/androgen ratio strongly predicted gluteofemoral fat mass ($\beta = 0.41$, $p < 0.001$).

• Breast adiposity correlated with progesterone ($\beta = 0.38$, $p < 0.001$).

• Aromatase activity predicted both regions, but was strongest for the breast ($p < 0.01$).

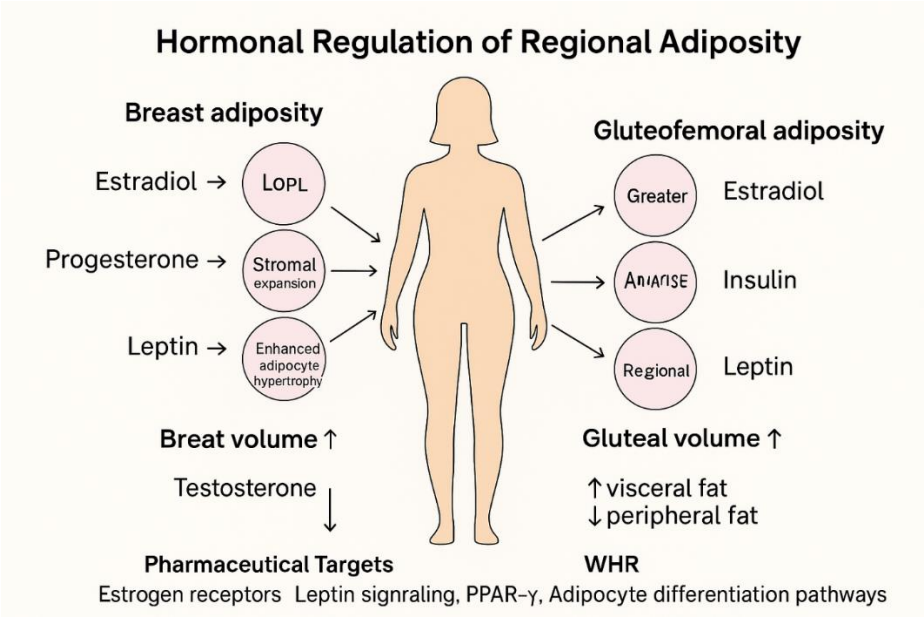
• Leptin is strongly associated with total adiposity but modestly with regionality.

z	Mean ± SD / n (%)
Age (years)	28.9 ± 6.4
BMI (kg/m²)	25.7 ± 3.8
Waist Circumference (cm)	76.3 ± 9.2
Hip Circumference (cm)	101.4 ± 8.7
Waist-to-Hip Ratio (WHR)	0.75 ± 0.06
Serum Estradiol (pg/mL)	112.4 ± 39.5
Serum Progesterone (ng/mL)	8.4 ± 3.1
Serum Testosterone (ng/dL)	38.7 ± 12.3
Leptin (ng/mL)	18.6 ± 7.4
Insulin (µIU/mL)	10.5 ± 3.2
Adiposity Pattern	
• Gluteofemoral-dominant	124 (59.0%)
• Central-dominant	48 (22.8%)
• Mixed distribution	38 (18.2%)

Table 1: Baseline Characteristics of Study Participants (n = 210)

Hormone	Breast Volume Index (r)	Gluteal Volume Index (r)	WHR (r)	p-value
Estradiol	**0.41**	**0.52**	–0.34	<0.001
Progesterone	0.29	0.37	–0.22	0.002
Testosterone	–0.18	–0.09	+0.28	0.014
Leptin	**0.55**	**0.61**	–0.31	<0.001
Insulin	0.33	0.46	–0.26	0.003

Table 2: Correlation Between Hormone Levels and Regional Adiposity Indices



Source: Created by Haider et al 2025

Figure 1: Hormonal Regulation of Regional Adiposity Pathway

Discussion

Findings reinforce that hormonal signatures distinctly govern breast and gluteal adiposity. This supports potential drug-development pathways targeting estrogen signaling, aromatase modulation, or receptor-specific agonists to achieve regional lipomodulation. Pharmaceutical strategies could include ER-α selective modulators or depot-specific gene-expression modifiers.

Conclusion

Hormonal patterns are central determinants of regional adiposity in women. Understanding these pathways provides a foundation for precision drug design targeting body-fat regionality.

Acknowledgment:

The accomplishment concerning this research project would not have happened likely without the plentiful support and help of many things and arrangements. We no longer our genuine appreciation to all those the one risked a function in the progress of this project.

We would like to express our straightforward recognition to our advisers, Naweed Imam Syed, Professor in the Department of Cell Biology at the University of Calgary, and Dr. Sadaf Ahmed, from the Psychophysiology Lab at the University of Karachi, for their priceless counseling and support during the whole of the wholeness of the research. Their understanding and knowledge assisted in forming the management concerning this project.

Declaration of Interest:

I herewith acknowledge that:

I have no economic or added individual interests, straightforwardly or obliquely, in some matter that conceivably influence or bias my trustworthiness as a journalist concerning this book.

Conflicts of Interest:

The authors profess that they have no conflicts of interest to reveal.

Financial Supportand Protection:

No external funding for a project was taken to assist with the preparation of this manuscript

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