Sapporo Medical Journal
Volume 57, Issue 12, December 2023

Hormonal Dynamics and Ovarian Follicle Quantity

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Abstract— Background: The primary function of the female ovary, which is correlated with hormone balance, is the creation of a mature and viable egg capable of fertilization, as well as subsequent embryo development and implantation. The ovarian reserve needs to be identified to diagnose and treat infertility. **Methods and Material:**descriptive, retrospective observational research. 230 people were included in the data from the roughly 500 patients who met the inclusion criteria and were admitted to the Sulaymaniyah Governorate's Royal Hospital (Infertility Center). The data were utilized to compare the robust regression model with the quantile regression model in medical data using statistical methods (SPSS24, Minitab19 and Eviews 10). The P-value and the Chi-Square test are performed to evaluate any significant correlations between variables. P-values less than 0.05 are considered significant. **Results:**The vast majority, 34.7% of those women older than 30, had fewer than 8 eggs, while 39.7% had between 8 and 15 eggs. There is a statistically significant relationship between (Age, TSH, FSH and PL) with the number of eggs because the p-value of these was less than the common alpha of 0.01. On the other hand, there is no statistical significance between LH and P4 on the number of eggs because the p-value of both variables was more than 0.05. **Conclusion:** The study concluded that the number of eggs was affected by age, follicle stimulation hormone, thyroid stimulating hormone,and prolactin.However, no relation between the number of eggs and the luteinizing and progesterone hormones could be found.

Keywords: Relationship, Eggs, Hormones, Royal Hospital, Sulaymanih Governorate

Introduction:

Forming a mature and viable egg capable of fertilization, with subsequent embryo development and implantation, is the main job of the female ovary(Sadler, 2022). The ovary has a limited supply of oocytes available for folliculogenesis at birth. "The ovarian reserve" refers to this limited pool of oocytes(Underwood et al., 2022). In order to diagnose and treat infertility, the ovarian reserve must be determined. The ovarian reserve will decrease as the ovary ages(Sargazi, S., Ahmadi, Z., Barani, M., Rahdar, A., Amani, S., Desimone, M. F., ... & Kyzas, 2022).

The ovaries generate a mature ovum during a process known as ovulation under the control of the hormones follicle-stimulating hormone (FSH) and luteinizing hormone (LH)(Luo et al., 2023). An oocyte matures and is discharged as an ovum around day 14 of the reproductive cycle. Even while the ovaries start to mature several oocytes every month, only one ovum is typically discharged per cycle. The size of the egg varies from woman to woman. Still, it typically measures between (3-5) centimetres, and the size of the ovaries greatly affects the likelihood of pregnancy for women who have small ovaries, leading to the issue of infertility or delayed conception(Krisher, 2022).

A girl can become pregnant through sexual activity as soon as she begins to ovulate. The first ovulation often occurs after the menarche, the start of the first menstrual period. If a woman's fertility diminishes after age 30 and worsens after age 35, 18 to 28 is her most fertile period(Moghadam et al., 2022). A third of women who wait until their mid-thirties to get pregnant will experience infertility issues; in modern times, the average age at which a woman conceives is 57(Osterman et al., 2022).

Thyroid issues are another factor influencing the ovary's functional reserve. One of the most prevalent endocrine issues in people of reproductive age is thyroid disease, which can lead to infertility and problems with menstruation and ovulation(Mazzilli et al., 2023).

Prolactin hormone (PLH) is another hormone that influences ovulation. Hyperprolactinemia is a well-known contributor to hypogonadotropichypogonadism(Ely & Hamilton, 2018); PRL acts on kisspeptin-1 neurons that express the PRL receptor (PRL-R), reducing kisspeptin-1 and GnRH release and producing anovulation(Chanson, P., & Maiter, 2022).

Progesterone is an endogenous steroid and progestogen sex hormone involved in the menstrual cycle, pregnancy, and embryogenesis of humans and other species. It is also used in women to support pregnancy and fertility and to treat gynaecological disorders. Then, p4 is an important part of infertility treatment. Moreover, Progesterone is produced in the Corpus Luteum of the overlies. This temporary gland follows the release of an egg from the ovary(Smith et al., 2022).

Children are viewed as the family's foundation in society and as the source of life's permanence. As a result, the husbands have a great desire to have children. An enhanced chance of getting pregnant can result from the early discovery of this issue, such as the lack or reduction of eggs and their treatment. This study was carried out for that reason.

Material and Methods:

In this retrospective observational study, our primary aim was to investigate the potential correlation between hormone levels and ovarian follicle count among a cohort of women aged 20-30 years who were undergoing in vitro fertilization (IVF) treatment at the Royal Hospital Infertility Center in Sulaymaniyah Governorate. Our study encompassed a dataset comprising approximately 500 patients, specifically focusing on 230 patients who met the defined inclusion criteria. Patients who were not receiving IVF treatment and those lacking complete hormone level records were deliberately excluded from our analysis.

Our study cohort consisted exclusively of these 230 women who were confronting the significant challenges posed by infertility while aspiring to initiate or expand their families. In our quest to comprehensively explore the factors influencing fertility outcomes, we meticulously collected and integrated a carefully curated set of variables into our analysis.

The first set of variables, integral to our investigation, included six explanatory variables. These were thoughtfully selected based on their relevance to the complex hormonal dynamics influencing fertility outcomes. Specifically, these variables encompassed Age, Thyroid-Stimulating Hormone (TSH), Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Prolactin (PL), and Progesterone (P4). Each of these variables was chosen due to its established impact on the reproductive system and its potential relevance to the number of eggs retrieved during infertility treatments.

The second set of variables revolved around our study's primary outcome variable: the number of eggs, scientifically known as oocytes. This crucial variable was a pivotal indicator of ovarian function and played a central role in assessing the efficacy of fertility interventions within our study population.

Our overarching objective was to systematically gather and analyze these data points to unveil the intricate interplay between the selected explanatory variables and the number of eggs, thereby advancing our comprehension of infertility and its potential treatment modalities. The insights derived from this research endeavour hold significant promise in guiding clinical decision-making, enhancing patient care, and contributing to the broader field of reproductive medicine.

Methodologically, our approach entailed utilising robust and quantile regression models. These analytical techniques were executed through various statistical software applications, including SPSS 24, Minitab 19, and Eviews 10. These models were specifically chosen to provide a comprehensive assessment of the relationship between hormone levels and ovarian follicle count, with a keen consideration for potential outliers and quantile-specific effects. Additionally, we employed statistical tools such as the P-value and Chi-Square test to assess significant associations among variables. In our analysis, a P-value of less than 0.05 was considered statistically significant, indicating a strong relationship between the variables under scrutiny.

Ethical considerations played a paramount role in the execution of our study. We obtained formal approval from the scientific and ethics committees at the College of Nursing, University of Sulaimani, ensuring strict adherence to ethical standards throughout our research process. Furthermore, formal authorization was diligently secured from the Royal Private Hospital before data collection, underscoring our unwavering commitment to ethical research practices and patient confidentiality.

Results:

The link between the response variable (number of eggs) and the explanatory variable is shown in Table (1). The vast majority of the women were older than 30. 34.7% of those women had fewer than 8 eggs, while 39.7% had between 8 and 15 eggs. While the majority, or 77.8% of women under 25, had more than 15 eggs. Therefore, the amount of eggs decreases as age increases.
Table 2 The association between the explanatory variable thyroid-stimulating hormone and the response variable (number of eggs) is shown in Table 2. 51.5% of women with TSH levels less than 1.1 have 8 to 15 eggs. 41.4% of women with TSH levels more than 3.0 have fewer than 8 eggs.

The association between the explanatory variable luteinizing hormone, and the response variable (number of eggs) is shown in Table (3). 40.4% of women with LH levels under 5 have more than 15 eggs. 45.5% of women with LH levels of more than 10 have fewer than 8 eggs. The majority of them, 36.4%, have 8 or more eggs when the LH level is normal, and 36.4% have less than 8.
The correlation between the response variable (number of eggs) and the explanatory variable, follicle-stimulating hormone, is shown in Table (4). 57.9% of women with FSH levels less than 5 have fewer than 15 eggs. While most women with FSH levels over 10 (74.1%) had less than 8 eggs, 40.5 percent had 8 to 15 eggs when the FSH level was normal.

Table (5) represents the relationship between the response variable (number of eggs) and the explanatory variable Prolactin (PL). Of women with a PL level that is lower than 10, 47.8% have 8-15 eggs. While women with a PL level of over 15, 41.8% have less than 8 eggs.When the PL level is at the normal rate, the majority of them 43.8% of them, have 8-15 eggs
Table (6) represents the relationship between the response variable (number of eggs) and the explanatory variable Progesterone 4 (P4). Of women with a P4 level that is lower than 0.3, 43.6% have 8-15 eggs. Meanwhile, the majority of women whose P4 level is more than 0.9, 64.1%, have more than 15 eggs. When the P4 level is at a normal rate, 41.7% of them have less than 8 eggs**.**

It can be seen from Table (7) that there is a statistically significant relationship between (Ages, TSH, FSH, PL) and the number of eggs because the p-value of these was less than the common alpha 0.01. Moreover, the result of coefficient age equals (-0.615072), which means that with each increase of a point of age, the number of eggs decreases by 0.615072 after constant other variables. The result of coefficient FSH and PL equal (-0.900721, -0.118607) respectively means that with each increase of a point of FSH and PL, the number of eggs decreases by 0.900721 and 0.118607 respectively after constant other variables. The result of coefficient TSH equals (0.572648) with each increase of a point of TSH, the number of eggs increases by 0.572648 after constant other variables. On the other hand, there is no statistical significance between LH and P4 on the number of eggs because the p-value of both variables was more than 0.05.

It can be seen from Table (8) that there is a statistically significant relationship between (Age, TSH, FSH and PL) with the number of eggs because the p-value of these was less than the common alpha 0.01. Moreover, the result of coefficient age equals (-0.658147); then, for each increase of one point of age, the number of eggs will decrease by (-0.658147) after constant other variables. The result of coefficient FSH and PL equal (-1.188523and -0.193645) respectively, meaning that for each increase of one point of FSH and PL, the number of eggs will decrease by (-1.188523and -0.193645) respectively after constant other variables. In other words, the result of coefficient TSH is equal

(1.076646), meaning that for each increase of one point of FSH, the number of eggs will grow by (1.076646) after constant other variables. In addition, there is no statistical significance between LH and P4 with the number of eggs because the p-value of the variable was more than 0.01.

Table (1): Relationship between the number of eggs and Age

Count	The number of eggs			
Age	< 8	8 – 15	> 15	Total
	N (%)	N (%)	N (%)	
< 25	2 (22.2)	0 (0.0)	7 (77.8)	9
25-30	4 (18.2)	0 (0.0)	18 (81.8)	22
> 30	69 (34.7)	79 (39.7)	51 (25.6)	199
Total	**75**	**79**	**76**	**230**

Table (2): Relationship between the number of eggs and TSH

Count	The number of eggs			
TSH	< 8	8 – 15	> 15	Total
	N (%)	N (%)	N (%)	
< 1.1	9 (17.3)	17 (51.5)	7 (21.2)	33
1.1 – 3.0	25 (25.5)	41 (41.8)	32 (32.7)	98
> 3.0	41(41.4)	21 (21.2)	37 (37.4)	99
Total	**75**	**79**	**76**	**230**

Table 3: Relationship between Numbers of the eggs and LH

Count	The number of eggs			
LH	< 8	8 – 15	> 15	Total
	N(%)	N(%)	N(%)	
< 5	24 (22.0)	41 (37.6)	44 (40.4)	109
5 – 10	16 (36.4)	16 (36.4)	12 (27.3)	44
> 10	35 (45.5)	22 (28.6)	20 (26.0)	77
Total	**75**	**79**	**76**	**230**

Table 4: Relationship between Numbers of the eggs and FSH

Count	The number of eggs			
FSH	< 8	8 – 15	> 15	Total
	N(%)	N(%)	N(%)	
< 5	1 (5.3)	7 (36.8)	11 (57.9)	19
5 – 10	31 (20.3)	62 (40.5)	60 (39.2)	153
> 10	43 (74.1)	10 (17.2)	5 (8.6)	58
Total	**75**	**79**	**76**	**230**

Table 5: Relationship between Number of eggs and PL

Count	The number of eggs			
PL	< 8	8 – 15	> 15	Total

	N(%)	N(%)	N(%)	
< 10	5 (21.7)	11 (47.8)	7 (30.4)	23
10 – 15	14 (19.2)	32 (43.8)	27 (37.0)	73
> 15	56 (41.8)	36 (26.9)	42 (31.3)	134
Total	**75**	**79**	**76**	**230**

Table 6: Relationship between the number of eggs and P4

Count	**The number of eggs**			
P4	**< 8**	**8 – 15**	**> 15**	**Total**
	N(%)	**N(%)**	**N(%)**	
< 0.3	14 (35.9)	17 (43.6)	8 (20.5)	39
0.3 – 0.9	53 (41.7)	47 (37.0)	27 (21.3)	127
> 0.9	8 (12.5)	15 (23.4)	41 (64.1)	64
Total	**75**	**79**	**76**	**230**

Table (7): Shows the Values of the Regression Coefficients According to the OLS Method

Explanatory variables	**Coefficient**	**Std. Error**	**t-Statistic**	**P-value**
Constant	43.38884	1.756718	24.69881	0.000
X_1 (Age)	-0.615072	0.035681	-17.2382	0.000
X_2 (TSH)	0.572648	0.113095	5.063412	0.000
X_3(LH)	-0.027777	0.071554	-0.3882	0.6982
X_4 (FSH)	-0.900721	0.081797	-11.0117	0.000
X_5 (PL)	-0.118607	0.031658	-3.74647	0.0002
X_6 (P4)	0.537975	0.527876	1.019131	0.3092

The model:

$$\widehat{number\ of\ the\ oocytes} = 43.38884 - 0.615072\ (\text{Age}) + 0.572648\ (\text{TSH}) - 0.027777\ (\text{LH}) - 0.900721\ (\text{FSH}) - 0.118607\ (\text{PL}) + 0.537975\ (\text{P4})$$

Table (8): Shows the Values of the Robust Regression Coefficients Using M-Huber

Explanatory variables	**Coefficient**	**Std. Error**	**t-Statistic**	**P-value**
Constant	47.05365	0.550616	85.45633	0.000
X_1 (Age)	-0.658147	0.011184	-58.84919	0.000
X_2 (TSH)	1.076646	0.035448	30.37255	0.0000
X_3(LH)	0.027828	0.022427	1.240786	0.2147
X_4 (FSH)	-1.188523	0.025638	-46.35808	0.0000
X_5 (PL)	-0.193645	0.009923	-19.51522	0.0000
X_6 (P4)	0.402559	0.165455	2.433044	0.0150

The model:

$$\widehat{Number\ of}\ oocytes = 47.05365 - 0.658147\,(\text{Age}) + 1.076646(\text{TSH}) + 0.027828(\text{LH}) - 1.188523\,(\text{FSH}) - 0.193645(\text{PL}) + 0.402559(\text{P4})$$

Discussion:

An extended post-reproductive period results from a large decline in human female fertility and reproductive lifetime with age. Compared to the previous several decades, maternal age has dramatically grown in industrialized countries, and at the same time, the age at which women have their first child has increased(Ely & Hamilton, 2018).Declining fertility is one of the main risks associated with increased maternal age because the human ovarian environment exhibits significant ageing-related changes very early in life (Moghadam et al., 2022).

According to universal consensus, the decline in the ovarian follicle reservoir and continuous exposure of the ovarian microenvironment to various ageing-related stimuli are the causes of the inverse association between age and fertility in females. However, it is still unknown whether oocyte quality affects an older woman's ability to reproduce(Babayev & Duncan, 2022).

Interestingly,invitrofertilizationofyoungfemaleoocytesandtransplantationintoage-matchedrecipientsrestorednormalyoungfemalepregnancyrates(Navot, D.; Bergh, R.A.; Williams, M.A.; Garrisi, G.J.; Guzman, I.; Sandler, B.; Grunfeld, 1991).Our research showed that the amount of eggs decreases as age increases. It can be shown that the majority, or 77.8% of women under 25, had more than 15 eggs. However, less than 8 eggs are present in 34.7% of women over 30. Our research is comparable to that of(Wasielak-Politowska & Kordowitzki, 2022), who found that both the amount and quality of eggs steadily decrease with age, which causes a fall in female fertility.

Each month, an egg can develop and be ovulated in women due to FSH. Unfortunately, women with high FSH levels frequently have poor or nonexistent responses to fertility drugs. When they try in vitro fertilization to get pregnant successfully, they can also have a poor likelihood of success. Some eggs may still be normal in a young patient with a little FSH increase.An increased FSH level indicates reduced ovarian reserve. Reduced follicles or eggs, frequently of low quality, are linked to a diminished ovarian reserve. According to statistics, it is rare that a woman who has continuously high FSH levels will be able to have a child.In recent research, 57.9% of women with FSH levels less than 5 have fewer than 15 eggs. While most women with FSH levels over 10 (74.1%) had less than 8 eggs, 40.5 percent had 8 to 15 eggs when the FSH level was normal.Our research is comparable to that conducted by Baker et al. (2015) The authors of the study discovered a significant decrease in the live birth rate with increasing follicle-stimulating hormone (FSH) dose regardless of the patient's age or how many oocytes were extracted(Baker et al., 2015).

The pituitary gland releases luteinizing hormone (LH). It regulates ovulation, uterine preparation for implantation of a fertilized egg, and ovarian synthesis of estrogen and progesterone. It also regulates the duration and timing of the female menstrual cycle(Mann et al., 2022).When serum LH levels rise, more androgen is produced, which impairs follicular function and lowers the viability of early embryos. Increased LH levels in the preovulatory stage may potentially harm subsequent events like conception and implantation.According to our research, it can demonstrate a negative relationship between LH and egg production. High LH rise with low egg surge and more LH with high egg number surge 40.4 percentage of women with LH levels under 5 have more than 15 eggs. 45.5% of women with LH levels of more than 10 have fewer than 8 eggs. Our research is in line with that of (Stanger & Yovich, 1985), who found that women undergoing IVF treatment who had elevated basal LH levels (more than one standard deviation from the mean) had significantly lower fertilisation rates. While (Alviggi et al., 2018) study findings areinconsistent with ours, they did not discover a significant difference between LH levels measured during conception and non-conception cycles. The change in LH levels between cycles that caused continued pregnancies and pregnancy loss was also not discovered.

Thyroid hormone levels influence ovulation and oocyte quality (Zhang et al., 2013). According to our research, there is a correlation between egg production and thyroid hormone (TSH). 51.5% of women with TSH levels less than 1.1 have 8 to 15 eggs. 41.4% of women with TSH levels more than 3.0 have fewer than 8 eggs.In humans, recipient clinical pregnancy favourably correlates with lower donor TSH levels, indicating oocyte-level impact (Karmon et al., 2016). Our findings are consistent with a 2003 study by Cramer et al., which found that women with higher TSH levels had lower fertilisation rates and lower-quality embryos. While our study contrasts with those conducted by(Chai J, Yeung WY, Lee CY, Li HW, Ho PC, 2014) and (Alexander et al., 2017), they could not show this, as shown by pregnancy rates.

Amenorrhea and infertility are known to be caused by hyperprolactinemia. Prolactin is thought to play a role in a number of physiological aspects of healthy reproduction, according to accumulating research(Iancu et al., 2023). Our study's coefficient PL equals (0.193645), which means that after holding all other variables constant, the number of eggs will fall by (-0.193645) for every point of PL that is increased.Our results are consistent with experimental studies that suggest high levels of prolactin may also have an impact on fertility by altering endometrial function and implantation due to structural and immunological variables(Duan Y., Liu X., Hou W., Deng M., Gao J., Zhou C., 2019). Several research studies assessed prolactin's impact on oocyte maturation,considering its presence in follicular fluid and the expression of the prolactin gene in ovarian granulosa cells, with mixed results.Oocyte competency and follicular fluid prolactin levels rarely showed a negative correlation. As a result, Lee et al. discovered increased prolactin concentrations in the follicular fluid of unfertilized oocytes(Lee M., Ben-Rafael Z., Meloni F., Mastroianni L., 1987), and (A. Reinthaller, J. Deutinger, P. Riss, E. Müller-Tyl, F. Fischl, 1987) demonstrated an association between progressed follicular maturation and decreasing follicular fluid prolactin. Other scientists challenged the function of monomeric prolactin in oocyte physiology and fertilization by finding no association between the follicular fluid prolactin level and IVF outcomes(Romão G.S., Ferriani R.A., Moura M.D., 2002).

Additionally, our findings demonstrate no statistically significant relationship between P4 and the quantity of eggs because the variable's p-value was greater than 0.01. While (Hill et al., 2017) showed no extra predictive value of progesterone to collected oocyte index (POI) to progesterone and several collected oocytes, our results are comparable to their findings.Our results do not agree with the research (Racca et al., 2018). The embryo utilization rate was much lower in the event of high progesterone levels, which suggests that the freeze-all technique would not be the best option in these instances. Recent studies have also linked excessive progesterone levels to poorer embryo quality. (Vanni et al., 2017)observed a negative association between the proportion of top-quality blastocysts and progesterone level, which supports the influence of high progesterone on embryo development ability.

Finally, a woman's fertility and capacity to become pregnant are significantly influenced by the quality of her eggs and the checking hormone. The best likelihood of an egg growing into an embryo, implanting in the uterus, and leading to a healthy pregnancy is high-quality eggs with regulated hormone levels. Testing for hormonal imbalances and low egg quality is crucial because these conditions are frequently curable with a change in lifestyle and medication.

Conclusion:

According to the study's findings, there is a substantial correlation between (Age, TSH, FSH, and PL) and egg number. In contrast,no statistically significant relationship exists between LH and P4 and egg count. Because the checking hormone and the quality of her eggs have a substantial impact on a woman's fertility and ability to become pregnant, testing them is crucial.

Strength and limitation

While the study provides valuable insights into the factors affecting ovarian reserve in a specific population, it has limitations related to its retrospective design, limited generalizability, potential confounders, and the need for further discussion on clinical implications. Researchers and healthcare professionals should consider these strengths and weaknesses when interpreting and applying the study's findings.

Acknowledgements
The author appreciates the Maternity Teaching Hospital and study participants, who assisted the researchers while gathering data.

Potential conflict of interest

There are no conflicts of interest, according to the authors.

Financial Support

We did not have any financial support for this study.

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