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Predictive Roles of Reproductive Hormones in Screening Human Males with Oligo Spermia

Enas Saad Sobeih[1], Department of Branch of Basic Sciences College of Dentistry, University of Al-Iraqia, Bagdadh, 11001, Iraq.
Shahad Kh. Al-Qaisi[2], Department of Nursing Techniques, Technical Institute of Baquba, University of Middle Technical, Diyala, 32001, Iraq.
Mayada Nazar Jabbar[3], Department of Biology, College of Science, University Diyala, Diyala, 32001, Iraq.
Corresponding author email: dr.enassabeeh@gmail.com

Abstract

Objective; Evaluation of the roles of testosterone, LH, FSH, and prolactin hormone indicators in the pathophysiology of patients with oligozoospermia.

Methods: This investigation was applied in Baghdad, Iraq, on people with oligozoospermia from June to September 2024. Fifty blood samples were collected from patients visiting outpatient clinics after being examined by a specialist (gynecologist). In addition, forty samples were taken from healthy individuals and considered as a control group. All hormones were measured in the study groups using the Snibe Maglumi 800 machine. SPSS v. 23.0 and Prism v. 6 statistical software programs were used for the analysis of our results.

Results; The present findings indicated that most patients fall within the age groups 21–30 years (28.0%), 31–40 years (22.0%), and 41–50 years (20.0%), while a smaller percentage fall within the ≤20 years (8.0%) and >60 years (10.0%) groups. LH, FSH, and prolactin levels were significantly increased ($p<0.05$) in patients compared to healthy individuals. In contrast, testosterone levels were significantly decreased ($p<0.05$) in patients compared to healthy individuals. ROC curve results showed that FSH achieved the highest sensitivity and specificity (71% and 75%), followed by prolactin (70% and 73%), testosterone (68% and 66%), and LH hormone (62% and 55%) at cutoff values of 7.12, 10.25, 1.965, and 5.25, respectively, in screening patients with oligozoospermia, with significant differences ($p<0.05$). There were positive and negative correlations among sexual hormones in oligozoospermia patients; however, these relationships were not significant ($p>0.05$). Finally, we found no significant variations ($p>0.05$) in the levels of sexual hormones across the age groups of patients.

Conclusion: The investigation revealed LH, FSH, and Prolactin levels were significantly increased, while testosterone levels were significantly decreased. ROC curve showed FSH scored the highest sensitivity and specificity, followed by Prolactin, testosterone, and lastly LH. In addition, there is no significant positive or negative correlation among reproduction hormones in oligozoospermia patients. There is no significant correlation between age and level of reproductive hormones.

Keywords: Reproductive Hormones, Human Males ,Oligospermia.

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1. Introduction

The standard definition of infertility is the failure to conceive after at least one year of consistent, unprotected sexual activity. Approximately 8% to 10% of couples worldwide are affected by this serious health problem [1]. About 50 million marriages worldwide are infertile, making it a global health issue [2]. According to the WHO statistics, infertility occurs in the absence of a clinical pregnancy following twelve months of frequent sexual intercourse without cover [3]. Iraq and the Middle East are generally underrepresented in the statistics on infertility. Middle Eastern nations have provided information on a variety of infertility cases and reasons [4].

Determining the forms and causes of sterility is critical in order to offer information that can shed light on regional variations in infertility trends. With 42 million people living there, Iraq is one of the most populous nations in the Middle East. According to reports, 18 Iraqi states have a 5.5% reproduction rate [5]. Abnormal genetics, neurological disorders, infections, trauma, endocrine (hormonal imbalance), gonadotoxins, and the formation of sperm antibodies are some of the causes of infertility in men [6].

Gonadotropin-releasing hormone (GnRH) is released by the brain, which also causes the pituitary gland to secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH). While LH indirectly promotes the generation of sperm through the manufacture of testosterone in Leydig cells, FSH directly enhances spermatogenesis by acting on the seminiferous tubules in Sertoli cells [7].

The pituitary gland secretes the hormone prolactin, which regulates GnRH through a feedback mechanism on the brain, thereby controlling the synthesis of LH and FSH. There is no established target organ or function for prolactin in male fertility. However, a latent function for prolactin in the control of male fertility is suggested by the presence of prolactin receptors on the choroid plexuses and the hypothalamus [8]. Via the hypersecretion of adrenal corticoids caused by prolactin or the inhibition of the release of GnRH through prolactin receptors on hypothalamic dopaminergic neurons, acute hyperprolactinemia can reduce testosterone production and fertility in men [9].

One testing method used to evaluate fertility in men is semen analysis. The inability to conceive after a year of unprotected sexual activity is known as infertility. A comprehensive physical exam, a full medical and sexual history, and semen assays are used to diagnose infertility in men. According to [10] the male factor has a substantial role in 30% of instances of infertility and is an explanation in approximately fifty percent of cases.

2. Methods section

2.1 Samples collection

The present investigation was conducted in Baghdad, Iraq, on people with oligozoospermia from June to September 2024. Fifty blood samples were collected from patients with low sperm counts (oligozoospermia) who visited outpatient clinics after being examined by a specialist physician. In addition, forty blood samples were taken from healthy individuals and considered as the control group. The ages of the participants ranged from 16 to 64 years.

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2.2 Techniques

The harvested blood was centrifuged in a centrifuge machine (5000 rpm for four minutes) to obtain serum. All hormones were measured in all participants using the Snibe Maglumi 800 with kits provided by Bio-Sources International (Camarillo, USA).

2.3 Statistical analysis

Sexual hormone indicators were expressed as Mean±SD. Student's t-tests were used to reveal the differences between oligozoospermia patients and healthy individuals for all hormones. ANOVA (Analysis of Variance) was used to measure differences among levels of these hormones across age groups. Age groups of oligozoospermia patients were expressed as frequency and percentage, and the differences among them were detected by the Pearson Chi-square test.

The receiver operating characteristic (ROC) curve was utilized to measure the area under the curve (AUC), cutoff, specificity, and sensitivity of sexual hormones. The Pearson correlation coefficient was used to detect the type and strength of associations among sexual hormones. A p-value of ≤0.05 was applied to reveal statistical variations. SPSS v. 23.0 and Prism v.6 statistical software programs were used for the analysis of our results.

3. Results Section

3.1 Distribution of patients according to age groups

The present outcomes showed that most patients with oligozoospermia were within the age groups 21–30 years (28.0%), 31–40 years (22.0%), and 41–50 years (20.0%), while a smaller proportion fell within the age groups ≤20 years (8.0%) and >60 years (10.0%). The differences among the age groups of patients were significant ($p<0.05$) as shown in Table 1.

Table 1: frequency and percentages of age groups of patients

Total number= 50		Count	Percent	P value
Age groups (years)	≤20	4	8.00%	p<0.01**
	21-30	14	28.00%	
	31-40	11	22.00%	
	41-50	10	20.00%	
	51-60	6	12.00%	
	>60	5	10.00%	

2. Levels of sexual hormones within study groups

The levels of LH, FSH, and prolactin in our study were significantly increased ($p<0.05$) in patients (11.56±0.49, 8.68±4.30, and 14.93±6.21) compared to healthy individuals (5.28±2.36, 6.35±1.66, and 9.98±3.87). On the other hand, testosterone levels were significantly decreased ($p<0.05$) in patients (1.58±0.49) compared to healthy individuals (2.71±1.02) as shown in Table 2 and Fig. 1

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Table 2: Comparative concentrations of sexual hormone indicators between patients versus healthy

Groups		N	Mean	Std. Deviation	P value
Testosterone (ng/ml)	Patients	50	1.58	0.49	P<0.05*
	Healthy	40	2.71	1.02	
LH (IU/mL)	Patients	50	11.56	4.45	P<0.05*
	Healthy	40	5.28	2.36	
FSH (IU/L)	Patients	50	8.68	4.30	P<0.05*
	Healthy	40	6.35	1.66	
Prolactin (ng/mL)	Patients	50	14.93	6.21	P<0.05*
	Healthy	40	9.98	3.87	

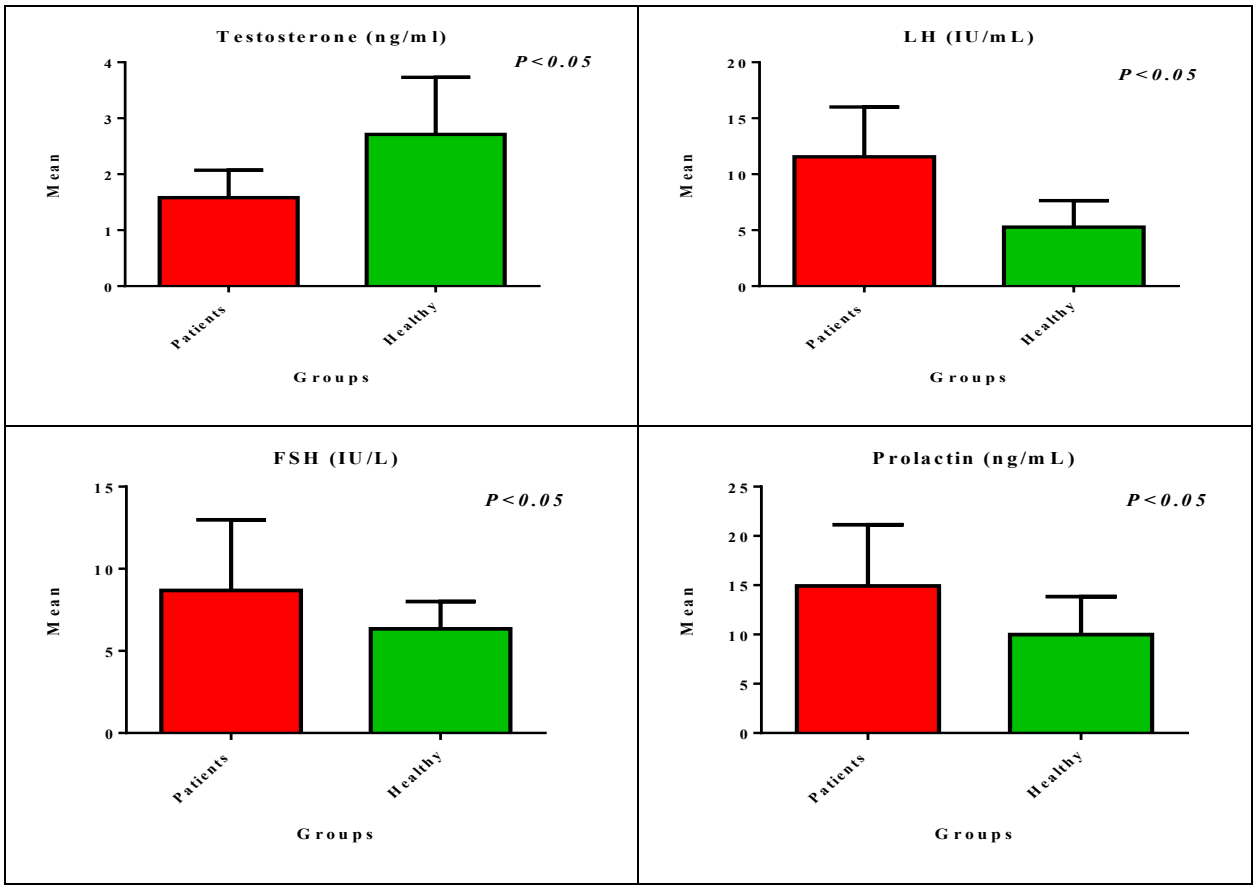

Fig. 1 Levels of reproductive hormones indicators for patients and healthy

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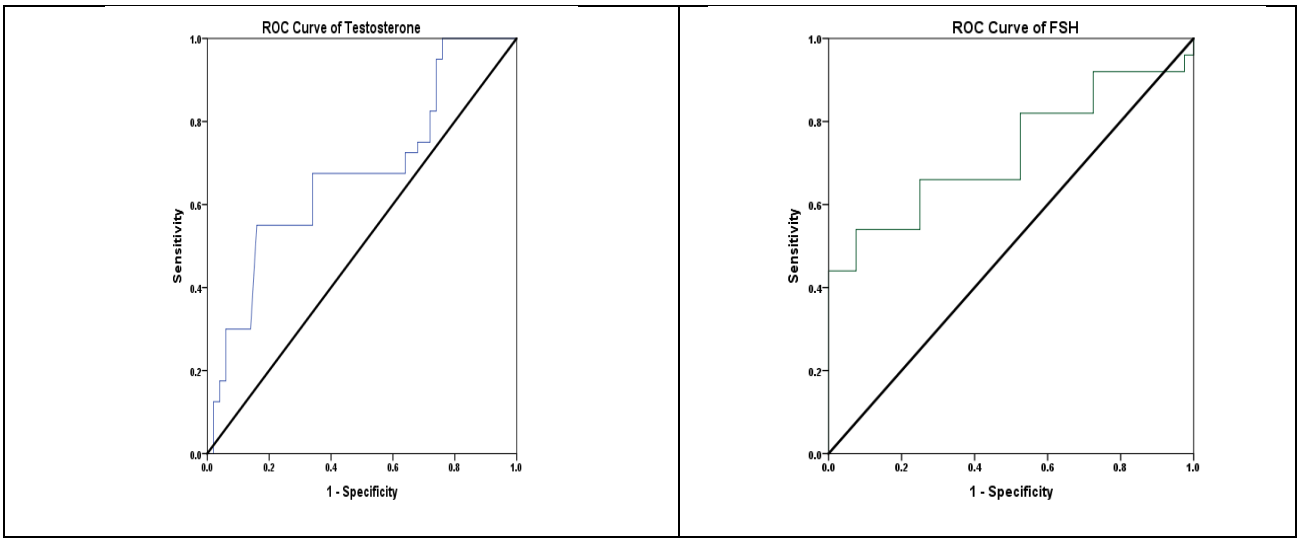
3. ROC curve of reproductive hormones indicators

Based on ROC curve results, our study showed that FSH achieved the highest sensitivity and specificity (71% and 75%), followed by prolactin (70% and 73%), testosterone (68% and 66%), and LH hormone (62% and 55%) at cutoff values of 7.12, 10.25, 1.965, and 5.25, respectively, in screening patients with oligozoospermia, with significant differences ($p<0.05$) as shown in Table 3 and Fig. 2.

Table 3: ROC curve, AUC, cutoff, sensitivity, and specificity of sexual hormone indicators in screening oligozoospermia patients and correlation relationships among sexual hormone indicators.

Variables	AUC*	S. E	p value	Cut off	Sensitivity %	Specificity %
LH	0.655	0.057	*P<0.05**	5.25	62	55
FSH	0.727	0.053	*P<0.05**	7.12	71	75
Prolactin	0.691	0.057	*P<0.05**	10.25	70	73
Testosterone	0.675	0.058	*P<0.05**	1.965	68	66
AUC= Area Under Curve						



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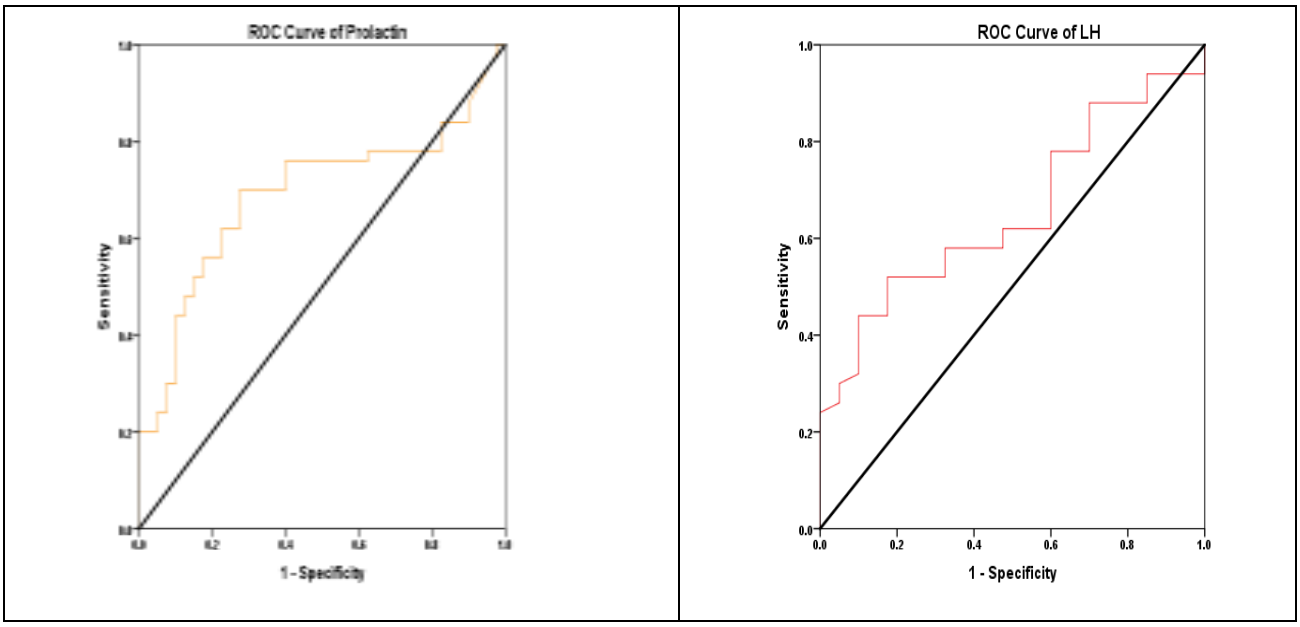

Fig. 2 ROC curve of sexual hormones

4. Correlation relationship among sexual hormones indicators

This study showed that there are positive and negative correlations among sexual hormones in oligozoospermia patients, but these relationships are not significant (P>0.05) (Table 4).

Table 4: correlation relationship among reproductive hormone indicators in patients

		Testosterone	FSH	Prolactin
Testosterone	Pearson correlation coefficient	1	-.078	-.248
	Probability		.592	.083
LH	Pearson correlation coefficient	-.205	.191	.190
	Probability	.154	.184	.185
Prolactin	Pearson correlation coefficient	-.248	.237	1
	Probability	.083	.098	

5. Relation of sexual hormones with patients age

Based on relation levels of sexual hormones with age groups, present findings do not reveal significant variations (p>0.05) between levels of these hormones and age groups of patients (Table 5)

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Table 5: comparative levels of reproductive hormones with age groups of patients

Age groups	Testosterone		LH		FSH		Prolactin	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
≤20	1.37	0.33	9.70	2.88	7.72	2.77	14.35	5.17
21-30	1.66	0.49	11.23	3.89	8.49	2.64	15.09	6.71
31-40	1.44	0.51	13.76	5.96	7.84	3.14	13.33	7.57
41-50	1.58	0.47	11.85	4.77	7.86	4.06	16.72	8.01
51-60	1.63	0.52	10.16	3.09	12.83	8.97	14.78	6.81
>60	1.26	0.49	12.44	5.24	8.54	2.42	17.08	7.01
P value	P>0.05		P>0.05		P>0.05		P>0.05	

6. Discussion

The proper operation of a complex network of hormones that regulate reproduction is necessary for spermatogenesis to occur, but changes in these hormone levels result in aberrant spermatogenesis and infertility. For this reason, accurate diagnosis and treatment of infertile guys depend on endocrinological evaluation.

The current results showed that almost 50.0% of all infertile males are between the ages of 21 and 40. This might be explained by the fact that Iraqi men often marry later, around their thirties, due to the country's economic circumstances. Additionally, in the age range of 21 to 40 years, Opheelia and Mohammed [11, 12] discovered that 52.0% and 54.0% of all infertile males, respectively, match the current study. Our results, however, disagree with those of [13], who found that 40% of infertile men were between the ages of 26 and 30. The disparity in incidence observed in our data compared to other studies could be attributed to various factors such as location, climate, socioeconomic status, racial distinctions, smoking, stress from radiation exposure, ethnicity, the time of year samples were collected, varicocele, infection, and genital deviations.

The likelihood of conception is 30% lower in males over 40 than in men under 30, according to the authors' findings. This can be attributed to factors such as the decline in semen volume, total sperm count, and sperm motility, or their ability to migrate toward the egg, as men age [14]. It has been demonstrated that gonadotropins are crucial for spermatogenesis and sperm development. Sperm properties have been found to have a substantial correlation with circulating concentrations of sex hormones [15]. Studies have discovered a negative relationship between spermiogram characteristics, including motility, morphology, sperm count, and blood FSH and LH levels. Others have reported a strong positive association between motility and testosterone levels [16].

The levels of testosterone in oligozoospermia patients were declined, while LH, FSH and prolactin were increased than healthy, and these outcomes were matched with the results. [11] The primary hormone in men is testosterone (T). The level of testosterone impacts a man's physical and emotional well-being in addition to his ability to conceive. Particularly in the creation of testosterone

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in Leydig cells, testosterone is recognized for its anti-inflammatory in nature and antioxidant characteristics [17]. It is vital to maintain a healthy lifestyle, practice often, and choose pharmaceutical therapies that may preserve testosterone and enhance serum levels since inadequate levels of testosterone can impair the quality of sperm and limit fertility Falling levels of testosterone are directly associated with health problems in males, although men often experience a loss in fertility and reproduction as they aged [18].

Consequently, raising testosterone levels to preserve normal reproductive health can improve a man's overall quality of life. Using medications derived from natural sources, testosterone-based therapies have become more popular recently for male reproductive issues. In addition to being linked to better semen quality and ROS scavenging ability, it can counteract problems with sperm quality and shield DNA from oxidative stress-induced damage [19]. Around 25% or more of doctors who administer testosterone to patients are ignorant that the drug may result in serious, perhaps permanent issues with sterility and fertility; also, patients are frequently not made aware of this possibility. [20] Exogenous testosterone suppresses the pituitary's ability to produce FSH and LH, which results in infertility. The lack of FSH and LH stops spermatogenesis and endogenous intratesticular testosterone synthesis.

According to Fink et al. [21], testosterone treatment can impair spermatogenesis in as little as 3.5 months. Supplementing with testosterone had little effect on male infertility patients' attempts to conceive. Clomiphene, which helps regulate FSH and LH phases, can assist patients who require testosterone treatment in retaining their fertility [22]. It will require time and there are no promises, but many individuals who become sterile while on testosterone medication will ultimately restore their sperm counts and fertility. According to the best-published statistics, men on testosterone treatment could anticipate a 90% recuperation in the production of sperm following a year, virtually a full recovery following a period of two years, and two-thirds of them recuperating in six months. [23] When it comes to sperm generation, LH and FSH collaborate tightly. To produce the right amount and quality of sperm, that hormone initiates the creation of testosterone. Low amounts of LH affect a man's libido and, eventually, his fertility. Elevated levels have the potential to harm testicles and have a deleterious effect on the generation of sperm [24].

The assessment of FSH and LH is helpful in the treatment of infertility among men. FSH is required for the initiation of spermatogenesis and the development of spermatozoa. Higher FSH concentrations in infertile men have been linked to severe oligozoospermia and azoospermia and are considered an accurate indicator of germinal epithelium destruction [25]. The primary controllers of germ development of cells are FSH and LH. Overall, an abundance of FSH and LH is necessary for the quantitative generation of spermatozoa. While LH indirectly promotes spermatogenesis through testosterone, FSH works directly on the seminiferous tubules. In spermatogonia, FSH is essential for promoting both mitotic and meiotic DNA synthesis. [26] LH and FSH were shown to be adversely correlated with the total motility of sperm in an earlier large-scale investigation. Only LH, nevertheless, demonstrated a separate negative connection with increasing sperm motility after correcting for FSH. [27] The researchers talked about how elevated LH and FSH levels might be a sign that the testicles aren't able to support healthy spermatogenesis [16].

Based on the author's knowledge, FSH treatment for males with idiopathic infertility enhances the amount of sperm and results in conception in one out of every four cases. The number of FSH-

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treated individuals needed to produce one pregnancy appears to be reduced in a clinical context as compared with data previously released, despite the predicted constraints due to real-world data research [28].

The current research revealed that patients had higher prolactin (PRL) concentrations than healthy individuals, and such results were consistent with those of Ambulkar et al. [29]. Hyperprolactinemia, or elevated blood prolactin levels, inhibits the anterior pituitary gland's pulsatile secretion of gonadotropins, harming spermatogenesis and male reproduction. The underlying cause of male infertility is significantly influenced by prolactin, which can also alter testicular function and semen output. Compared to earlier research, the incidence of hyperprolactinemia is higher in the prior investigation. Furthermore, analyses of endocrine indicators revealed that male infertile patients with hyperprolactinemia had significantly negative effects on endocrine variables. The mean blood levels of testosterone, LH, and FSH significantly decreased in the infertile group compared to the healthy group as the degrees and seriousness of hyperprolactinemia increased [30]. PRL stimulates human spermatozoa's ability to use glucose and fructose, adenylate cyclase activity, and ATPase activity in the discharge. However, this affects the spermatozoa's mobility and fertilization potential through its energy metabolism [31].

Results from a meta-analytic method indicated that there was an independent relationship between the rates of erectile dysfunction and either lower testosterone (T) levels or high prolactin (PRL) levels (HPRL). Moreover, a portion of the erectile dysfunction problem was resolved when PRL levels returned to baseline. In the clinical environment, HPRL had no discernible effect on the severity of erectile dysfunction (ED). Lastly, restoring healthy sexual activity can be achieved by treating PRL levels (HPRL); however, its impact on erections is not significant [9]. Therefore, to provide appropriate treatment and increase fertility rates, it is imperative to conduct a timely hormonal assessment of the male component in infertile couples. Despite advancements in the identification of male infertility, certain factors remain unclear [3]. In recent years, both doctors and male patients have benefited from being able to estimate the likelihood of male infertility without semen analysis. Researchers believe that individuals at risk for male infertility can benefit from monitoring by medical providers other than reproductive specialists. Eventually, an AI (artificial intelligence) forecasting system will be implemented in clinical laboratories and medical check-up facilities. For instance, it will be feasible to assess adult males' potential for infertility solely by measuring their serum hormone levels without requiring semen analysis. People would be directed to an infertility institution if anomalies were discovered [33]. Based on the hormonal assessment, our study showed that FSH and prolactin are the best indicators for diagnosing male infertility due to their high sensitivity and specificity.

Prior research showed that individuals with non-obstructive azoospermia (NOA) had a subsequent sperm retrieval (SR) rate of 61.3% for microsurgical testicular sperm extraction (mTESE). In NOA individuals undergoing mTESE, the T/LH ratio, bilateral testicular sizes, and pretreatment serum FSH levels were favorable predictors of successful sperm retrieval (SR) in both the favorable and negative SR groups. The inclusion of the T/LH ratio as a clinical prognosticator, in addition to conventional criteria, may increase the prediction accuracy of SR prospects among individuals with azoospermia, even if there are no clear-cut indicators of successful SR following surgery [34]. A prior investigation [13] demonstrated that serum PRL is recognized as an indicator of

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male infertility because of its high sensitivity and specificity (85% and 87%). These results were higher than those of our study, which indicated that PRL had a sensitivity and specificity of 70% and 73%, respectively. According to earlier research, prolactinoma and macroprolactinoma are indicated by PRL levels >250 µg/L and >500 µg/L. Hormone levels appear to moderate prediction in the presence of pituitary masses but no macro lesions for reduced PRL values in participants of both genders with high PRL at sequential sampling [35].

In individuals with male reproductive problems, inadequate spermat8ogenesis is linked to elevated blood levels of prolactin, FSH, and LH, along with low blood levels of testosterone. Furthermore, oligozoospermia in sterile males was substantially correlated with higher blood prolactin concentrations and lower serum testosterone concentrations [36]. Finally, the current study found no significant differences in hormone levels among patients across different age groups.

7. Conclusion

The investigation revealed LH, FSH and Prolactin levels were significantly increased, while testosterone levels were significantly decreased. ROC curve showed FSH scored the highest sensitivity and specificity, followed by Prolactin, testosterone and lastly LH. In addition, there is non- significant positive and negative correlation among reproduction hormones in oligozoospermia patients. There is no significant correlation between age and level of reproductive hormones.

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