



Analysis of Biochemical Indicators in Female Infertility

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Abstract

Background: Infertility affects a significant proportion of women worldwide, with various underlying causes. The biochemical assessment of hormonal and metabolic indicators can provide critical insights into the etiologies of female infertility. Biochemical indicators play a crucial role in diagnosing and understanding female infertility. Hormonal profiles, metabolic conditions, and specific biomarkers like AMH provide valuable information about ovarian function, reproductive health, and underlying pathologies. Integrating these markers into a comprehensive diagnostic approach can improve the accuracy of infertility assessments and guide personalized treatment strategies. Future research should focus on longitudinal studies to validate these biomarkers and explore their potential in therapeutic interventions. This study aims to systematically analyze the role of specific biochemical markers in diagnosing and understanding female infertility.

Aim: The primary aim of this study is to evaluate the relationship between various biochemical indicators and female infertility, focusing on hormones, metabolic profiles, and other relevant biomarkers. Additionally, the study seeks to identify potential biomarkers that could enhance diagnostic accuracy and therapeutic strategies.

Material and Method: A case-control study design was employed for this investigation conducted in the Department of Obstetrics and Gynecology. The study included 80 patients diagnosed with various conditions—20 with PCOS, 15 with BOH, 20 with endometriosis, and 25 with ovarian insufficiency. These patients were compared with 80 matched healthy controls. A specially designed proforma was used to gather information on personal, medical, and reproductive histories. Hormone levels for follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), and testosterone (T) were measured in the participants.

Results: The data suggests that women with PCOS, endometriosis, and OI experience higher oxidative stress, as indicated by elevated LPO levels. The increased SOD activity in these groups reflects a compensatory response to this oxidative stress, except in the case of OI, where SOD activity is not significantly elevated. Increased protein levels in the study groups (PCOS, endometriosis, and OI) compared to controls might indicate an inflammatory or stress-related response in these conditions. The FSH levels elevated in BOH, indicating reduced ovarian reserve. Other groups show relatively normal levels. LH Varies widely among conditions, with the lowest levels in endometriosis, possibly suggesting hypogonadism or other issues. E2 Lower in PCOS and endometriosis compared to controls, with OI showing the highest levels. T Elevated in PCOS and endometriosis, indicating possible hyperandrogenism. P Significantly lower in endometriosis and PCOS, with potential implications for reproductive health.

Conclusion: The analysis of biochemical indicators in female infertility reveals significant disruptions in oxidative stress and hormonal regulation across various infertility conditions. Elevated oxidative stress, along with hormonal imbalances in FSH, LH, E2, T, and P, highlights the complexity of infertility and its underlying mechanisms. These insights are crucial for developing targeted diagnostic

and therapeutic strategies. Addressing oxidative stress through antioxidants, managing hormonal imbalances with appropriate therapies, and considering lifestyle modifications can improve fertility outcomes. Continued research into the biochemical and molecular aspects of infertility will enhance our understanding and lead to more effective and personalized treatments for women facing infertility challenges

Keywords: Female Infertility, Biochemical Indicators, Hormonal Markers, Metabolic Profiles, Ovarian Reserve, Anti-Müllerian Hormone, Polycystic Ovary Syndrome, Diagnostic Biomarkers.

Introduction

Infertility is a multifaceted medical condition that affects a significant portion of the global population, with female infertility being a prominent concern. It is defined as the inability to conceive after a year of regular, unprotected sexual intercourse, or the inability to carry a pregnancy to term. Infertility can arise from a variety of physiological, anatomical, and biochemical factors, making it essential to explore all potential underlying causes. Biochemical indicators play a crucial role in understanding and diagnosing female infertility. These indicators are measurable substances in blood, urine, or other bodily fluids that reflect the biochemical status of various physiological processes. By analyzing these markers, healthcare professionals can gain insights into hormonal imbalances, metabolic disorders, and other physiological disruptions that may be contributing to infertility.^{1,2}

Hormones are chemical messengers that regulate numerous functions in the body, including reproductive processes. Imbalances in reproductive hormones, such as estrogen, progesterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH), can disrupt ovulation, fertilization, and implantation, leading to infertility. For instance, elevated levels of FSH may indicate diminished ovarian reserve, while abnormal progesterone levels can affect the uterine lining's ability to support embryo implantation. FSH is crucial for ovarian follicle development and regulation of menstrual cycles. Elevated FSH levels can indicate diminished ovarian reserve or premature ovarian insufficiency.³ LH triggers ovulation and

supports the corpus luteum. An imbalance can disrupt the menstrual cycle and ovulation. Estrogen is essential for the regulation of the menstrual cycle and preparation of the endometrium for implantation. Progesterone prepares the endometrium for implantation and supports early pregnancy. Low levels can lead to difficulties in maintaining a pregnancy. AMH is produced by ovarian follicles and provides an estimate of the ovarian reserve.^{4,5}

Metabolic and endocrine disorders, such as polycystic ovary syndrome (PCOS) and thyroid dysfunction, are commonly associated with infertility. PCOS is characterized by elevated levels of androgens and insulin resistance, which can lead to irregular ovulation and impaired fertility. Thyroid hormones, including thyroxine (T4) and triiodothyronine (T3), are critical for maintaining a healthy reproductive system; their dysregulation can impact menstrual cycles and ovulation. Insulin and glucose metabolism are closely linked with reproductive health. Insulin resistance is commonly associated with PCOS, which affects ovulation and fertility. Thyroid hormones (T3, T4, and thyroid-stimulating hormone [TSH]) are critical for normal menstrual function and ovulation. Prolactin is involved in lactation and can affect the menstrual cycle and ovulation.^{6,7}

The evaluation of biochemical indicators involves various diagnostic tests and assays. Blood tests can measure hormone levels, including those related to ovarian function and overall reproductive health. Urine tests may be used to assess luteinizing hormone surges that indicate ovulation. Additionally, advanced

techniques such as serum anti-Müllerian hormone (AMH) levels provide valuable information about ovarian reserve and reproductive potential.⁸ Techniques such as ultrasonography for follicle tracking and serum biomarkers for assessing specific conditions. Understanding biochemical parameters is essential for diagnosing the specific causes of infertility and developing appropriate treatment strategies. For example, hormone replacement therapies or medications that regulate hormone levels can be prescribed based on the biochemical profile of the patient. Furthermore, identifying underlying conditions through biochemical analysis allows for targeted interventions, improving the chances of conception and successful pregnancy.^{9,10}

The analysis of biochemical indicators in female infertility offers a detailed understanding of the complex interactions between hormonal and metabolic factors affecting reproductive health. By examining these biochemical markers, clinicians can better diagnose, manage, and treat female infertility, ultimately supporting women in their journey toward achieving a successful pregnancy. This approach not only enhances the precision of infertility treatments but also contributes to personalized healthcare strategies that address the unique needs of each individual.^{11,12}

Material and Methods

A case-control study design was employed for this investigation, conducted in the Department of Obstetrics and Gynecology. The study included 80 patients diagnosed with various conditions—20 with PCOS, 15 with BOH, 20 with endometriosis, and 25 with ovarian insufficiency. These patients were compared with 80 matched healthy controls. A specially designed proforma was used to gather information on personal, medical, and reproductive histories. Hormone levels for follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), progesterone (P), and testosterone (T) were measured in the participants.

Inclusion and Exclusion Criterion

To be included in the study, infertile participants had to be diagnosed with one of the following conditions: polycystic ovary syndrome (PCOS), bad obstetric history (BOH), endometriosis, or ovarian insufficiency. The study excluded infertile women who had primary or secondary amenorrhea, tubal obstruction, fibroids, or other similar conditions.

Biological Samples

- **Blood Samples:** Collected in sterile tubes, typically for serum analysis. Commonly used to assess hormone levels, metabolic markers, and other biochemical indicators.
- **Urine Samples:** Collected in clean, dry containers, used for assessing ovulation through luteinizing hormone (LH) surges.

Analytical Instruments

- **Hormone Assay Kits:** Include enzyme-linked immunosorbent assays (ELISA), radioimmunoassays (RIA), or chemiluminescent immunoassays (CLIA) for quantifying hormone levels such as FSH, LH, estrogen, progesterone,.
- **Ovulation Predictor Kits:** Used to measure LH levels in urine to detect ovulation.

Sample Collection and Preparation

- **Blood Collection:** Blood is collected via venipuncture into appropriate tubes, such as those containing anticoagulants for plasma or serum tubes. The samples are then centrifuged to separate the serum or plasma from cellular components.
- **Urine Collection:** Urine is collected mid-stream in clean containers and may be tested immediately or stored at 4°C for short periods before analysis.

Hormone Level Measurement:

- **ELISA:** Enzyme-linked immunosorbent assays are used to measure specific hormone concentrations. This involves adding samples to wells coated with antibodies specific to the hormone, followed by detection with enzyme-linked secondary antibodies and colorimetric or chemiluminescent substrates.

- **RIA:** Radioimmunoassays involve radiolabeled hormones and are used to measure concentrations by detecting the radioactivity of bound and unbound hormones.

Ovulation Detection

- **Urine LH Testing:** Utilizes ovulation predictor kits to detect LH surges in urine. The presence of LH is indicated by a color change in the test strip, correlating with the time of ovulation.

Quality Control and Validation

- **Calibration:** Regular calibration of assay instruments with standards to ensure accuracy.
- **Controls:** Use of control samples with known concentrations to verify assay performance and reproducibility.
- **Validation:** Ensuring that methods and instruments are validated for their intended use through performance checks and validation studies.

Statistical Analysis

The information gathered in this analysis was statistically analysed. The standard deviations and mean were determined. The significance and non-significance of each parameter is determined using students t' values to draw probabilities. The research subjects and healthy control subjects were compared statistically. The values in the tables and figures are mean + standard error.

Result:-

The study involved 80 individuals with infertility caused by conditions such as polycystic ovarian syndrome (PCOS), endometriosis, bad obstetric history (BOH), and ovarian insufficiency (OI), along with 80 healthy controls matched for age. Following approval from the infertile participants, the study was conducted. Data collected included general information, personal history such as age, age at marriage, menstrual cycle details, number of children, and family medical history.

Table No.-1 Show the Anti stress indices in control and study groups

| Parameters | Control (n=80) | Study Groups | | | |
|--------------------------------|-------------------|----------------|-------------------------|---------------|--------------|
| | | PCOS (n=20) | Endometriosis (n=20) | BOH (n=15) | OI (n=25) |
| LPO (nmol/ml) | 2.89±0.22 | 5.14±0.21 | 4.88±0.38 | 4.63±0.42 | 5.10±0.46 |
| SOD activity (U/mg protein) | 1.45±0.25 | 2.32±0.18 | 3.77±0.22 | 3.46±0.18 | 1.48±0.13 |
| Protein levels (mg/100µl) | 0.23±0.36 | 0.43±0.041 | 0.37±0.044 | 0.32±0.026 | 0.39±0.046 |

The control group has the lowest LPO levels, indicating less oxidative damage. The groups with PCOS, endometriosis, BOH, and ovarian insufficiency (OI) show significantly higher LPO levels, with PCOS and OI showing the highest values, suggesting increased oxidative stress in these conditions. The control group has the lowest SOD activity, which might seem counterintuitive but suggests a balance in oxidative stress. The PCOS, endometriosis, and BOH groups show higher SOD activity, reflecting an enhanced antioxidant response to

increased oxidative stress. OI has similar SOD activity to the control group, suggesting a potential deficiency or dysfunction in the antioxidant defense mechanism. Protein levels are higher in the PCOS, endometriosis, and OI groups compared to the control group, suggesting increased protein content, which may be related to inflammatory or stress responses. The BOH group has intermediate levels of protein, indicating a different level of systemic change compared to the other conditions.

Table No-2 shows the Hormones levels in control and study groups.

| Parameters | Study Groups | | | | |
|--------------|-------------------|----------------|-------------------------|---------------|--------------|
| | Control (n=80) | PCOS (n=20) | Endometriosis (n=20) | BOH (n=15) | OI (n=25) |
| FSH (mIU/ml) | 5.65±1.55 | 7.44±1.74 | 4.52±0.58 | 31.17±10.15 | 5.61±1.51 |
| LH (mIU/ml) | 23.41±8.21 | 15.79±1.62 | 3.71±1.48 | 6.71±1.11 | 11.66±5.21 |
| E2 (pg/ml) | 130.5±46.46 | 82.29±18.50 | 83.77±13.81 | 100.4±17.05 | 155.4±60.57 |
| T (ng/dl) | 39.54±13.17 | 69.31±10.44 | 80.38±12.50 | 51.84±14.07 | 63.41±07.66 |
| P (ng/ml) | 4.72±1.58 | 2.50±0.59 | 0.40±0.13 | 3.48±1.14 | 1.18±0.42 |

Controls and women with PCOS and OI have similar FSH levels. Endometriosis shows slightly lower levels, while women with BOH exhibit significantly elevated FSH levels. Controls show the highest LH levels, which are typical of normal menstrual cycles. PCOS shows lower LH levels compared to controls, which may indicate disrupted hormonal regulation. Endometriosis has the lowest LH levels, suggesting potential hypogonadism or disruption of the normal reproductive axis. Estradiol levels are lower in PCOS and endometriosis compared to controls, which might reflect disrupted ovarian function or altered estrogen production. BOH has intermediate levels, while OI has the highest levels, potentially indicating compensatory or aberrant estrogen production due to impaired ovarian function. Testosterone levels are elevated in PCOS and endometriosis compared to controls, indicating potential hyperandrogenism. Progesterone levels are significantly lower in women with endometriosis and PCOS compared to controls, which may affect the luteal phase and overall reproductive function. Women with BOH have intermediate levels, and those with OI have the lowest progesterone levels, possibly reflecting impaired luteal function.

Discussion

The analysis of biochemical indicators in female infertility provides crucial insights into the underlying physiological and pathological processes. This discussion will elaborate on the implications of various biochemical markers, explore their roles in different infertility conditions, and discuss their relevance for diagnosis and treatment. Elevated LPO levels in conditions like PCOS, endometriosis, and ovarian insufficiency (OI) compared to controls

indicate increased oxidative stress. Among these, PCOS and OI exhibit the highest LPO levels. Increased oxidative stress can damage cellular components, including lipids, proteins, and DNA, which may adversely affect ovarian function and overall reproductive health. In PCOS, oxidative stress may contribute to insulin resistance and hormonal imbalances. In endometriosis and OI, oxidative stress might exacerbate inflammatory responses and impair ovarian function. SOD activity is notably higher in women with PCOS, endometriosis, and bad obstetric history (BOH), reflecting an attempt to counteract increased oxidative stress.^{13,14} However, OI shows similar SOD activity to controls, which may indicate a less effective antioxidant response. Elevated SOD activity in PCOS and endometriosis suggests that these conditions are associated with increased oxidative stress, which the body attempts to neutralize through enhanced antioxidant defenses. In contrast, the lack of elevated SOD activity in OI may point to a dysfunction in the antioxidant defense system or an overwhelmed capacity to mitigate oxidative damage.^{15,16}

Elevated FSH levels in the BOH group indicate a compromised ovarian reserve or premature ovarian insufficiency. The levels in PCOS, endometriosis, and OI are similar to controls, with PCOS showing slightly elevated levels. High FSH levels in BOH suggest that the ovaries are not responding adequately to hormonal stimulation, potentially due to a reduced number of viable follicles. In contrast, normal FSH levels in other conditions suggest that ovarian reserve may be less affected or that the hormonal axis is functioning relatively normally.¹⁷

Lower LH levels in PCOS and endometriosis might indicate disrupted ovarian function or

hypothalamic-pituitary-gonadal axis abnormalities. In PCOS, it could be due to altered hormonal regulation, while in endometriosis, it might reflect a disruption in the normal reproductive axis. The intermediate levels in BOH and OI suggest a less pronounced disruption in LH secretion. Reduced estradiol in PCOS and endometriosis could indicate disrupted ovarian follicle development and impaired estrogen production. In PCOS, this might be due to hormonal imbalances and anovulation. Elevated estradiol in OI might reflect a compensatory mechanism or aberrant estrogen production, which could be associated with disrupted ovarian function or an altered hormonal environment.¹⁸ High testosterone levels in PCOS and endometriosis are consistent with their clinical presentations of hyperandrogenism, which contributes to symptoms like hirsutism and acne. In PCOS, elevated testosterone is linked to disrupted folliculogenesis and menstrual irregularities. The lower testosterone levels in BOH and intermediate levels in OI suggest that androgen levels are less aberrant in these conditions. Low progesterone levels in PCOS and endometriosis reflect impaired luteal phase function and insufficient endometrial preparation for implantation. In PCOS, this is often due to anovulation. The lower progesterone levels in OI may indicate a compromised luteal phase or inadequate corpus luteum function, affecting fertility.¹⁹

Biochemical markers like LPO, SOD activity, and hormonal profiles provide valuable diagnostic information. Elevated LPO and altered hormone levels can help identify oxidative stress, hormonal imbalances, and reproductive dysfunction associated with different infertility conditions. Continued research into these biochemical indicators can refine our understanding of infertility mechanisms and improve diagnostic and therapeutic strategies. Exploring the interactions between oxidative stress and hormonal regulation could lead to novel treatment approaches for managing female infertility.²⁰ The analysis of biochemical indicators in female infertility reveals significant differences in

oxidative stress markers and hormonal profiles among various infertility conditions. Elevated oxidative stress and disrupted hormonal levels are characteristic of conditions like PCOS, endometriosis, and ovarian insufficiency. These findings underscore the importance of a comprehensive biochemical evaluation in diagnosing and managing female infertility and highlight the need for targeted interventions to address this underlying issues.²¹

Conclusion:

The analysis of biochemical indicators in female infertility reveals significant disruptions in oxidative stress and hormonal regulation across various infertility conditions. Elevated oxidative stress, along with hormonal imbalances in FSH, LH, E2, T, and P, highlights the complexity of infertility and its underlying mechanisms. These insights are crucial for developing targeted diagnostic and therapeutic strategies. Addressing oxidative stress through antioxidants, managing hormonal imbalances with appropriate therapies, and considering lifestyle modifications can improve fertility outcomes. Continued research into the biochemical and molecular aspects of infertility will enhance our understanding and lead to more effective and personalized treatments for women facing infertility challenges.

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