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Impact of Hormonal Imbalance and Cytokines Inflammatory Response on Leukemia Inhibitory Factor Gene (LIF) Dysregulation in Endometriosis Pathogenesis

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ABSTRACT

INTRODUCTION: The development of endometrial glands in extrauterine locations, primarily in the female pelvis, is referred to as "endometriosis." Its occurrence in the general female population is 6–10%; however, among those who are in pain or are infertile, it can reach 35–60%. While the exact cause of endometriosis is unknown, immunological, hormonal, genetic, and environmental factors are most likely involved. Understanding the genetic, hormonal, and immunological components is important for enhancing diagnostic accuracy and treatment efficacy.
METHODS: In 160 patients aged 21 to 45, a case-control study was conducted that included blood collection, immunological serum analysis, RNA isolation for cDNA synthesis, and LIF gene expression.
RESULT: The function of chronic inflammation was suggested by the higher levels of and IL-6 seen in endometriosis-affected women in this research. Women with endometriosis showed dysregulated ovarian activity, as evidenced by greater FSH and decreased AMH levels in comparison to controls. The test group's LIF gene downregulation may have contributed to the development of endometriosis.
CONCLUSION:
The findings of this study highlight the multifaceted nature of endometriosis, involving genetic, inflammatory, and hormonal factors. The downregulation of the LIF gene and the associated increase in inflammatory markers

may serve as potential biomarkers for the disease and provide opportunities for early diagnosis and targeted therapy. The hormonal alterations observed further complicate the clinical conditions of endometriosis, suggesting that treatment strategies like, endocrine and immunological aspects of the diseases.

Key word; Biomarkers, cytokines, dysregulation, Endometriosis, gene regulations, inflammations.

INTRODUCTION

The term "endometriosis" refers to the development of endometrial glands and epithelium at extra-uterine sites, which are normally located within or adjacent to the female pelvis's visceral and peritoneal surfaces, though they may occur in the pelvic connective tissue and, less commonly, in other anatomical regions (Signorile et al.,2015). In the overall female population, the incidence of endometriosis is 6–10%; however, among women who suffer from pain, infertility, or both, this increases to 35–60% (Signorile et al., 2012). It is a common gynaecological condition affecting 20–50% of women struggling with fertility (Signorile et al.,2015).) displays a wide range of pain symptoms, including infertility, persistent pelvic discomfort, dyspareunia and mild to severe dysmenorrhea (Muñoz-Hernando et al., 2015). Even though the exact cause of endometriosis is unknown, it is most likely a result of a complicated relationship between immunological, hormonal, genetic, and environmental variables. Retrograde menstruation is widely acknowledged as a permissive factor for the development of endometriosis (Rai et al 2010).

An easy blood test for diagnosing and predicting endometriosis could potentially resolve these issues and significantly enhance women's health. The complexity of non-surgical diagnosis may contribute to current discrepancies. Although diagnostic laparoscopy is the standard for endometriosis diagnosis, it is an intrusive procedure that poses possible danger such as severe injury to blood vessels or the colon (Malutan et al.,2015). Its suggested that immune system abnormalities result in development of endometriosis, especially when it comes to immune-related cells and macrophages in the peritoneum that produce different chemicals, mostly cytokines and growth factors (Mihalyi etal.,2010). This process involves an immune-inflammatory response that stimulates both immune cells and endometriotic implants, resulting in significant production of angiogenic products, growth factors, and cytokines (Kubatova etal.,2013). Conversely, endometriosis has also been associated with systemic immunological changes, including the activation of peripheral blood monocytes that release large amounts of cytokines (Carmona et al., 2012).

Diagnostic delays and misdiagnosis are common due to the heterogeneous presentation of the condition. Current treatments offer only symptomatic relief and lack targeted interventions. Thus, understanding these dynamics is crucial for accurate diagnosis and effective treatment strategies. This study aims to elucidate the roles of genetic, hormonal, and immunological factors in the pathogenesis of endometriosis. By investigating LIF (Leukaemia Inhibitory Factor) gene expression alongside hormonal fluctuations and inflammatory responses, it seeks to uncover their interrelationships. Shedding light on these mechanisms could lead to personalised approaches for diagnosis and treatment, ultimately improving outcomes and quality of life for affected patients,

METHODS

The **case-control study** involved 160 participants, comprising 80 cases and 80 controls, all aged between 21 and 45 years. The study population take in 160 women, divided into 2 groups: **Group-I (Endometriosis Group)** included 80 women with a regular menstrual cycle, confirmed endometriosis through histopathological analysis, and no history of pelvic infections, autoimmune diseases, or neoplastic conditions. **Group-II (Control Group)** included 80 young, healthy, non-pregnant women between the ages of 21 and 45 who revealed no signs of endometriosis, either clinical or paraclinical.

History of pelvic surgeries, cancer, suspected malignancy, adenomyosis, leiomyoma, or premature ovarian failure and those who had used ovarian suppressive drugs or anti-inflammatory medications in the preceding six months were also excluded. Additionally, subjects diagnosed with an inflammatory or infectious condition within the last 5-6 months were excluded from the study.

The samples were selected based on the inclusion and exclusion criteria. Following informed consent, venous blood samples were collected after an 8–10 hour fast. Before breakfast, a total of 5 ml of venous blood was collected from each participant and blood was centrifuged, and the resulting serum was kept at -20°C for analysis. Data was collected using a **pre-structured questionnaire,** which included general and anthropometric data (weight, height), age, and onset of symptoms. The ratio of weight (kg) to squared height (m2) was used for determining the body mass index (BMI).

For genetic analysis, RNA isolation was performed from blood samples using a commercially available RNA extraction kit (spin column). Complementary DNA (cDNA) synthesis was conducted using reverse transcription. Total RNA (50 ng) was reverse transcribed using the Origin cDNA synthesis kit with an RNase inhibitor, following the manufacturer's instructions.

The gene expression level of the LIF gene was assessed using 2X-Real Time PCR (RT-PCR) master mix (including SYBR Green): 4× 1 mL. The temperature and time programmes, and protocol for expression analysis, were performed with the Bio-Rad CFX-Opus-96 machine and Bio-Rad CFX Maestro software. Specific primers for LIF gene (**F** -TCAGACAAGGCTTGGCAACCCA, **R**-GCCACATAGCTTGTCCAGGTTG) expression were provided by ORIGINDIAGNOS (Eurofins Genomics India) Relative LIF expression was calculated using the $2^{(-\Delta\Delta Ct)}$ method.

Enzyme linked Immunosorbent Assay (ELISA) investigated, Antibody-coated ELISA kits were used for detecting IL-6 (Interleukin-6), AMH (Anti-Mullerian Hormone), and FSH (Follicle Stimulating Hormone) in human blood serum and plasma. The kits used were: Human IL-6, Human AMH, and FSH. The quantitative sandwich enzyme immunoassay technique was employed to measure the levels of these biomarkers. Samples were tested according to the ELISA kit instructions, with temperature and time programmes for the assay examined by the Thermo Scientific Multiskan S.C. machine and Skanit RE 6.1.1 software (Additional File 4: Table-1).

The statistical analysis employed in this study involved a comprehensive analysis of various demographic, lifestyle, and health-related factors associated with infertility. Initially, descriptive statistics were calculated to summarize the characteristics of the study group (N=80) and control group (N=80), including frequencies and percentages for categorical variables and means with standard deviations for continuous variables. Inferential statistics were performed by comparing continuous variables with the independent samples t-test and assessing associations between categorical variables using the Chi-square test. Additionally, binary logistic regression analysis was conducted to evaluate the relationship between multiple predictors and the endometriosis, allowing for the adjustment of potential confounding factors. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for each predictor to quantify the strength of associations. A Receiver Operating Characteristic (ROC) curve analysis was also performed to evaluate the diagnostic accuracy of predictor of endometriosis, Furthermore, Pearson correlation coefficients were computed to explore the relationships between inflammatory markers and other biochemical parameters. The statistical analyses were performed using appropriate software, ensuring robust and reliable results that contribute to the understanding of endometriosis. The significance level was set at $p < 0.05$ Data analysis was performed using "jamovi 2.5.3".

ETHICAL CONSIDERATION

The study was conducted following approval from the **Institutional Ethics Committee of Genetika (IECG)** under letter number [Reg No. EC/NEW/INST/2022/2847]. **Informed consent** was collected before sample collection. Participants were recruited from various infertility clinics, maternity **centers,** and **Genetika, the Centre for Advanced Genetic Studies** in Trivandrum, Kerala, India.

RESULTS

The findings indicated a significant association ($p < 0.05$) in demographic variable measurements between the control and test groups, were shown in Table-1. The mean age of participants in test group was 33.5 ± 7.1 years, compared to 38.4 ± 5 years in the control group, with predominance of females in both groups. Moreover, the test group exhibited a higher BMI compared to the control group, further emphasising the demographic differences identified. These findings highlight the importance of demographic factors in understanding the observed variations between the test and control populations.

		Test (N=80)	Control (N=80)	P value*
Socioeconomic status**				
	Lower	4(5%)	9(11.3%)	
	Middle	43(53.8%)	61(76.3%)	
	Upper	33(41.3%)	10(12.5%)	<0.001
H/o Endometriosis***				
	Yes	70(87.5%)	18(22.5%)	
	No	10(12.5%)	62(77.5%)	<0.001
H/o Diabetes				
	Yes	27(33.8%)	1(1.3%)	
	No	53(66.3%)	79(98.8%)	<0.001
H/o Thyroid Disorder				
	Yes	14(17.5%)	0(0%)	
	No	66(82.5%)	80(100%)	<0.001
Sugar intake				
	Not-Restricted	68(85%)	50(62.5%)	
	Restricted	12(15%)	30(37.5%)	0.001
Water intake per day				
	Low	1(1.3%)	6(7.5%)	
	Moderate	55(68.8%)	27(33.8%)	
	High	24(30%)	47(58.8%)	<0.001
Regular food from home				
	Yes	63(78.8%)	74(92.5%)	
	No	17(21.3%)	6(7.5%)	0.013

TABLE-1: Association of demographic, lifestyle parameters for patients aged between 21-45 years categorized by different diagnostic subgroups. *p <0.001 indicates statistically significant, **socio economic status classification follows XYZ scale, ***history of endometriosis was determined by based on medical reports.

The table shows, the test group also had significantly higher rates of H/o endometriosis, sugar intakes (87.5% v/s 22.5% p < 0.001, 85% vs 62.5% p < 0.001.).H/o Diabetes, H/o Thyroid Disorder were significantly more in the test group (p < 0.001). Test group also showed lower rates of socio-economic status, water intake per day (1.3% vs 7.5%, p < 0.001). and regular food from home (78.8% v/s 92.5%, p < 0.013).

	Test (n=80)	Control (n=80)	p-value
Age	33.5 ± 7.1	38.4 ± 5	<0.001
Birth Order	1.9 ± 1.2	2.5 ± 2	0.030
Educational level	12.6 ± 3	11.9 ± 3.7	0.176
Duration of Married life (Yrs)	9.8 ± 7.1	17.7 ± 8.3	<0.001
Age at Marriage	23.7 ± 4.3	20.7 ± 6.5	0.001

Age of Husband	36.5 ± 7.3	44.8 ± 11.5	<0.001
Age at menarche	12.9 ± 1	13.5 ± 1.1	<0.001
No. of Pregnancy	2.5 ± 0.9	2 ± 0.9	<0.001
No. of Abortions	2.1 ± 0.8	0 ± 0	<0.001
BMI	27.9 ± 3.7	24.5 ± 3	<0.001
Fasting Blood Sugar	130.5 ± 58.6	87.8 ± 11.7	<0.001
Serum Triglyceride	146.1 ± 36.8	107.8 ± 18.4	<0.001
Serum Total Cholesterol	224.1 ± 46.7	166 ± 24.2	<0.001
Serum HDL Cholesterol	41.1 ± 5.9	48.2 ± 4.7	<0.001
Serum LDL Cholesterol	153.8 ± 42.8	75.7 ± 38.5	<0.001
T3	94.6 ± 36.5	124.7 ± 23.3	<0.001
T4	6.5 ± 3.1	7.6 ± 2.5	0.012
TSH	6.5 ± 4.9	2.3 ± 1.2	<0.001
FSH	23.9 ± 3.4	17.2 ± 3.1	<0.001
AMH	0.94 ± 0.7	5.09 ± 2.97	<0.001
LIF	0.46 ± 0.37	0.84 ± 0.38	<0.001
IL 6	7.16 ± 7.16	2.02 ± 1.58	<0.001

TABLE 2: Association of Demographic, Physiological, Biochemical, and Genetic Parameters, BMI (Body Mass Index), T3(Triiodothyronine)T4 (Thyroxine), TSH (Thyroid Stimulating Hormone). FSH (Follicle Stimulating Hormones, AMH (Ant- Mullerian Hormone) LIF (Leukemia Inhibitory Factor), IL-6 (Interleukin-6). *P-Values are presented as means ± standard deviations. Statistical significance was determined using independent sample t-tests with p-values < 0.05 considered significant.

In genetic analysis, Table 1 revealed that IL-6 levels higher in the endometriosis group (7.16 ± 7.16 pg/mL v/s 2.02 ± 1.58 pg/mL, p < 0.001). Clinically, IL-6 levels above 5 pg/mL have been linked to more severe endometriosis and poorer treatment outcomes. The mean level in the endometriosis group exceeds this threshold, suggesting that IL-6 could serve as a valuable prognostic marker.

The observed difference in AMH levels (0.94 ± 0.7 ng/mL in the endometriosis group v/s. 5.09 ± 2.97 ng/mL in controls, p < 0.001) carries significant clinical implications. AMH levels below 1 ng/mL are generally associated with diminished ovarian reserve. The mean level in the endometriosis group falls just below this clinically important threshold, indicating that these patients may have reduced fertility potential and might benefit from earlier fertility preservation interventions or more aggressive treatment strategies.

FSH levels were significantly higher in the endometriosis group (23.9 ± 3.4 IU/L v/s. 17.2 ± 3.1 IU/L, p < 0.001). Clinically, FSH levels above 10 IU/L are often considered elevated, potentially indicating decreased ovarian function. The substantially higher mean in the endometriosis group suggests that these patients may have more pronounced ovarian dysfunction, which could impact fertility treatment planning and success rates.

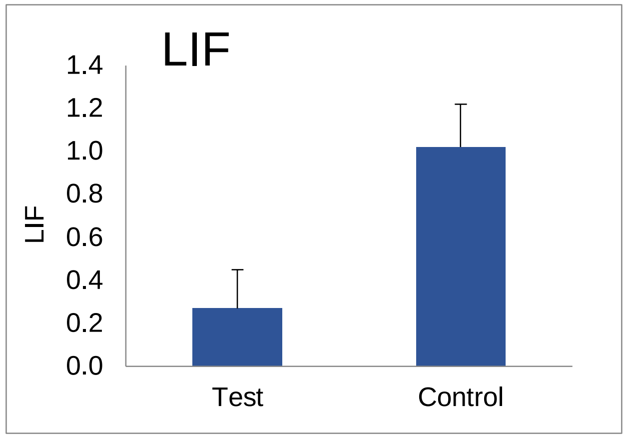


FIGURE 1: Comparison of LIF Levels between Test and Control Groups

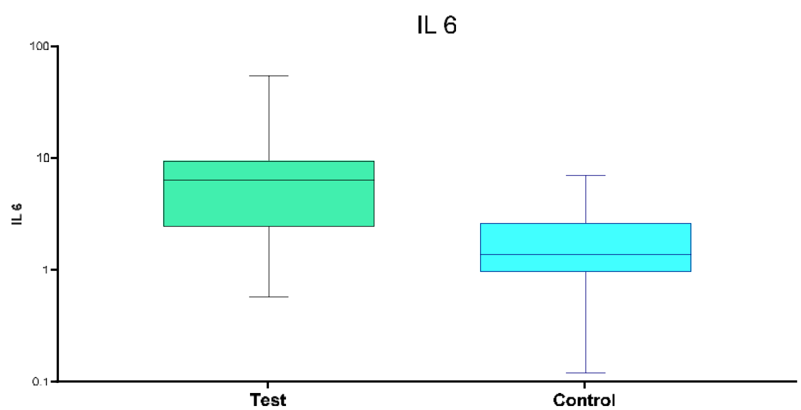


FIGURE 2: Comparing IL-6 Levels Between Test and Control Groups

The bar diagram (FIGURE-2) shows, the Control group exhibits higher levels of LIF than the Test group, with bars extending to about 1.2 and 0.2, respectively, suggesting reduced LIF in the Test group.

The box plot (FIGURE-3) of IL-6 reveals that the Test group has a higher median level (1.6) and greater variability, with whiskers ranging from 0.1 to just above 10, compared to the Control group's median of 0.8 and whiskers from slightly below 0.5 to approximately 2. This indicates that the Test group has increased IL-6 levels due to the applied condition or treatment.

	B	S.E.	p-value*	Odds ratio (OR)	95% C.I.for OR	
					Lower	Upper
Sugar intake	1.03	1.113	0.355	2.80	0.32	24.82
IL6	3.428	1.481	0.021	30.82	1.69	562.16
AMH	5.679	1.176	<0.001	292.66	29.19	2934.45
LIF	3.517	1.147	0.002	33.68	3.56	318.76
Constant	27.108	6.49	<0.001	0.00		

TABLE-3: Binary Logistic Regression Analysis of Parameters between Test and Control Groups. The logistic regression analysis reveals that association between the predictors and outcomes. B-(Regression coefficient), SE-(Standard Error) OR- (Odds Ratio),95% C.I for OR (95% confidence interval) constant-in regression analysis, it represents the value of response or dependent variable in regression equation associated predictors or independent variable equal to zero, *Statistical significance is indicated by p-values, AMH-(Anti- Mullerian Hormone), IL-6 (Interleukin-6).

The logistic regression analysis evaluates relationship between predictors and outcomes. Coefficients estimate predictors impact with p-values determining significant. Odd ration shows outcome changes.

Multivariate analysis employing binary logistic regression, identified AMH, LIF, and IL-6 as independent predictors of endometriosis. Specifically, AMH (Adj. OR: 292.66, 95% CI: 29.19-2934.45, p<0.001), LIF (Adj. OR: 33.68, 95% CI: 3.56-318.76, p=0.002), and IL-6 (Adj. OR: 30.82, 95% CI: 1.69-562.16, p=0.021) emerged as significant predictors. Confidence interval (CI) provides the range of uncertainty for odds ratios.

The study investigated the levels of IL-6, FSH, AMH, and LIF gene expression in women with and without endometriosis. Significantly elevated level of IL-6 was observed in women with endometriosis compared to control group and supporting the role of chronic inflammation in pathogenesis of the condition. Higher levels of FSH and lower levels of AMH in the test group indicated potential ovarian function dysregulation. Furthermore, the downregulation of LIF gene expression in the test group suggested a possible regulatory role of LIF in endometriosis development.

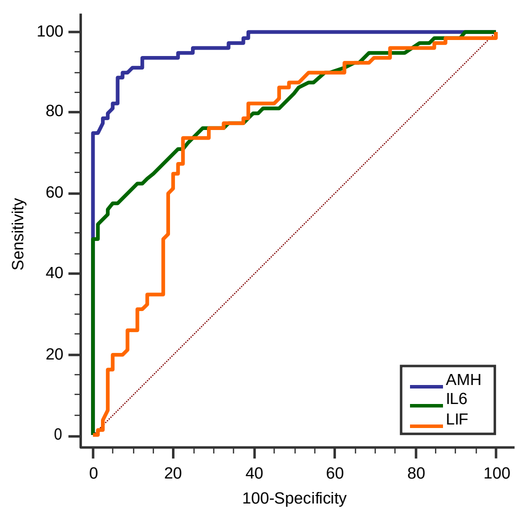


FIGURE 3: ROC Curve Analysis for Predicting Endometriosis Using Various Parameters. AMH (Ant-Mullerian Hormone) LIF (Leukemia Inhibitory Factor), IL-6 (Interleukin-6)

The ROC curve analysis (Figure 5) provides a valuable assessment of the diagnostic accuracy of various biomarkers for predicting endometriosis, quantified by the Area Under the Curve (AUC), by plotting true positive rate (Sensitivity) against false positive (1- Specificity). The AUC values for the different parameters indicate their effectiveness as diagnostic tools. AMH (Anti-Müllerian Hormone) exhibits the highest AUC value, signifying its superior ability to differentiate between the test and control groups. IL-6 (Interleukin-6) shows the second highest AUC, indicating it is the next most effective biomarker in distinguishing between the groups. LIF (Leukemia Inhibitory Factor) has the lowest AUC value among the biomarkers, suggesting it is the least effective in this analysis. The high AUC value for AMH reflects its optimal performance in correctly identifying positive cases while minimizing false positives. IL-6 also demonstrates robust performance but with slightly lower efficacy compared to AMH, outperforming LIF but falling short of AMH and IL-6. LIF, although less effective, still contributes to the discriminatory power of the model. Overall, the ROC curve analysis establishes that AMH is the most reliable biomarker for the study, with IL-6, and LIF following in descending order of diagnostic efficacy, as evidenced by their respective AUC values.

	AUC	SE	95% CI
AMH	0.969	0.0109	0.929 to 0.990
IL-6	0.828	0.0324	0.760 to 0.883
LIF	0.759	0.0392	0.685 to 0.823

TABLE 4: AUC of ROC curves of various parameters, AMH (Anti- Mullerian Hormone) LIF (Leukemia Inhibitory Factor), IL-6 (Interleukin-6). AUC-(Area Under the Curve) SE- (Standard Error) 95% CI-(95% Confidence Interval)

The ROC curve analysis provides a comprehensive evaluation of the diagnostic effectiveness of biomarkers: AMH, IL-6, and LIF. The Area Under the Curve (AUC) values indicate that AMH is the most effective biomarker, with an AUC of 0.969, suggesting excellent diagnostic ability. This is further supported by its low standard error (SE) of 0.0109 and a narrow 95% confidence interval (CI) ranging from 0.929 to 0.990, indicating high precision and reliability. IL-6 follows with a good diagnostic ability, reflected by an AUC of 0.828, and SE of 0.0324, and a 95% CI of 0.760 to 0.883, showing reasonable precision. LIF with AUC values 0.759 was, demonstrate fair to good diagnostic abilities, LIF has an SE of 0.0392 and a 95% CI of 0.685 to 0.823, indicating moderate precision. Overall, AMH stands out as the most reliable biomarker, followed by IL-6, and LIF, in descending order of effectiveness (Table 3).

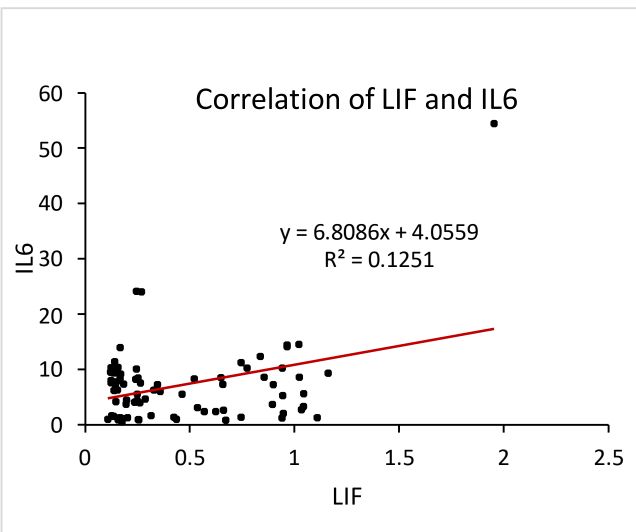
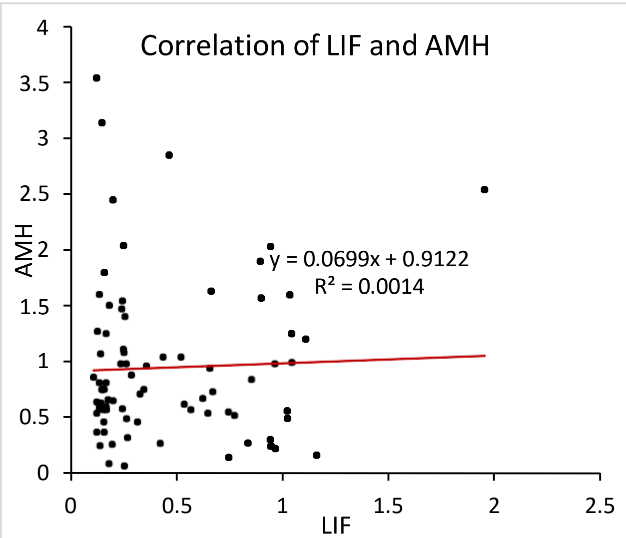


FIGURE 4 : Scatter plot showing correlation of LIF gene expression with IL-6



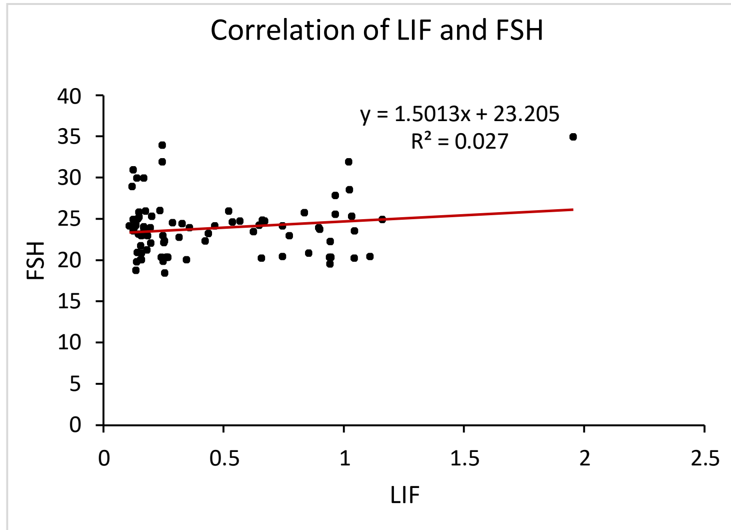


FIGURE 5& 6: Scatter plot showing correlation of LIF gene expression with AMH, and FSH

The regression analysis (Figure: suggests a slight positive relationship between LIF and AMH, with LIF being a weak predictor of AMH levels. For LIF and FSH, there is a positive but not strong correlation. Finally, the relationship between LIF and IL-6 shows a moderate positive correlation, making LIF a moderate predictor of IL-6 levels.

DISSCUSSION

There are several hypothesized etiopathogenic mechanisms causing endometriosis. Among them, genetic variability and mutations in many genes are being firmly proposed as endometriosis risk factors; they can be passed down via families. A further exciting hypothesis about the genesis of endometriosis is the impact of metabolic modifications, evaluated by metabolomics research (Moini et al.,2022). Although endometriosis is associated with increased concentration of T-cells, B-cells, activated macrophages and inflammatory cytokines an immunological/inflammatory etiology has been suggested (Kang et al., 2014). diminished production of proteins associated with interleukin. The IL -6 family plays a crucial role in determining endometrial receptivity. This includes leukemia inhibitory factors that have been identified. Proposed as potential explanation for the sub-fertility observed in cases of endometriosis (Moberg et al 2015). When endometriosis lesions form in the peritoneum, they release a various of cytokines that trigger the influx of immune cells, both of which exacerbate the inflammatory microenvironment (Nirgianakis et al.,2021).

In our study, IL-6 indicates a higher level of inflammation in the test group, which could be related to the endometriosis and other disorders under investigation. Increased IL-6 levels are correlated with a number of physiological and biochemical variations, indicating IL-6's function in inflammation and the underlying cause of disease.

Over the past few years, a great deal of scientific work done to investigate inflammatory biomarkers in endometriosis patients (Zhou et al., 2019) and researched as prospective targets for therapy or as non-invasive biomarkers for diagnosis (Nirgianakis et al., 2021), serum levels of IL-6 of endometriosis have the subject of inconsistent findings, however most of the investigations were positive. In the event of endometriosis, a significant rise in IL-6 levels and the early stages of endometriosis, anterior reports revealed substantially increased IL-6 levels than in the healthy group (Mier-Cabrera et al., 2011). Furthermore, IL-6 and pain were found to be correlated in one investigation, and cytokine expression was linked to endometriosis recurrences (Velasco et al., 2010).

In the present study, IL-6 is a pro-inflammatory cytokine often associated with inflammatory conditions, including endometriosis. Elevated IL-6 levels may reflect the severity of the inflammatory process. The high IL-6 levels in our endometriosis group suggest that this cytokine may serve as a useful prognostic marker in assessing disease severity and guiding treatment. It is thought that interleukin 6 may be involved in development and maintenance of ectopic endometrial tissue. Although IL-6's function in the pathophysiology of endometriosis has been well explored, there has been inconsistent detection of IL-6 in endometriosis patients' blood and peritoneal fluid levels. (Moini et al., 2013).

LIF receptors were found on the blastocyst, endometrium and trophoblasts. Furthermore, there is some indication that ectopic pregnancies in the fallopian tubes may be related to LIF and LIF receptor expression (Krishnan et al., 2013). The expression of human endometrial LIF is regulated on the cycle, reaching its peak during the implantation-receptive stage. During this time, secreted LIF protein may be seen in uterine flushes. TNF-alpha (Tumor Necrosis Factor- alpha) interleukin 1b, and hCG therapy all cause an increase expression of LIF and igp-130 receptor in endometrium. Moreover, the placenta, glandular and luminal epithelium, as well as the blastocyst, all have the LIF receptor. certain human reproductive diseases are linked to a notable decrease in LIF expression (Franasiak et al., 2014). LIF is a crucial component for the start of embryo implantation in humans. Nevertheless, infertility can also be seen without LIF deficiency (Terakawa et al.,2011).

In our findings, it is possible that there is abnormality or dysfunction in the processes where LIF is engaged, as suggested by the test group's considerable decreasing LIF expression. This may be a sign of pathological states or disease states that the test group members are experiencing. Although total LIF levels were lower in the study group, this shows that as IL-6 levels increase, LIF levels also tend to increase. This association demonstrates that these cytokines' roles in inflammation and immunological responses are interconnected.

Serum AMH is a superior predictor of ovarian response in endometriosis than FSH. Low AMH values signify insufficient reaction. AMH levels influence the choice of infertility treatments. Patients with endometriosis show elevated FSH and decreased AMH. In order to predict ovarian response, AMH is essential. In addition, it predicts the hyperstimulation reaction in females with increased FSH (Yoo et al., 2011). Endometriosis may impact ovarian response but not follicle reserves, as shown by stable AMH levels. Basal FSH levels can predict ART success in affected women (de Carvalho et al., 2010).

In this study, AMH is a hormone produced by ovarian follicles and is a marker of ovarian reserve. Low level of AMH was associated with reduced fertility potential. In endometriosis, low AMH levels suggest that patients with endometriosis may have a reduced ovarian reserve, which may affect their fertility and necessitate early interventions or more aggressive treatment strategies.These correlations suggest interactions between inflammatory marker IL-6 and parameters (LIF, FSH, T3, AMH), highlighting their potential impact on reproductive health and endocrine function. This detailed analysis provides insights into the complex relationships between the parameters, which can be critical for understanding the underlying mechanisms of reproductive and metabolic disorders.

` The findings of elevated IL-6 level of women with endometriosis align with previous research indicating the inflammation of the disease. Chronic inflammation may contribute to the maintenance of endometrial implantation and other symptoms associated with endometriosis. The observed dysregulation of FSH and AMH levels further underscores the complexity of endometriosis, implicating ovarian dysfunction as a potential factor in disease pathogenesis. The downregulation of LIF gene expression in the test group is an intriguing finding that warrants further investigation. LIF has implicated in various cellular processes, including inflammation and proliferation of cell, and its dysregulation play a role in endometriosis development. Overall, these results contribute to understanding the multifactorial nature of endometriosis and highlight potential targets for future therapeutic interventions aimed at addressing the underlying mechanisms of the disease. Further study is needed to elucidate the specific roles of IL-6, FSH, AMH, and LIF in endometriosis pathophysiology and to develop targeted treatments that can improve outcomes for affected individuals

CONCLUSION

In summary, although these results greatly advance our knowledge of endometriosis, more investigation is necessary to define the precise functions of IL-6, FSH, AMH, and LIF in the pathophysiology of the disease. This greater comprehension will be essential for creating more specialized and efficient therapies that are suited to address the various facets of this complicated illness. The findings offer strong proof that the pathophysiology of endometriosis involves persistent inflammation, ovarian dysfunction, and dysregulation of gene expression in endometriosis. To clarify the precise functions of IL-6, FSH, AMH, and LIF in the development of illness and investigate their potential as therapeutic targets, more investigation is necessary.

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Conflict of interest: we declare no conflicts of interest.

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