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The Impact of Mitochondrial Dysfunction in human oocytes on Embryo quality and Conception rates in IVF patients with varying stages of Endometriosis

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Abstract

Background: *Endometriosis is a chronic, estrogen-dependent gynecological condition that is closely linked to infertility. Although significant progress has been made in assisted reproductive technologies (ART), including in vitro fertilization (IVF), women with endometriosis frequently encounter challenges such as poor oocyte quality, impaired embryo development, and lower pregnancy rates. Emerging evidence suggests that mitochondrial dysfunction, particularly through reduced ATP production and mitochondrial DNA (mtDNA) deletions, plays a critical role in the reproductive difficulties observed in these patients.*

Aim: *The aim is to evaluate the impact of mitochondrial dysfunction on oocyte quality, embryo development, and IVF outcomes in women with endometriosis, comparing them with a control group of women without endometriosis.*

Methodology: *A prospective cohort study was conducted over three years (2021-2024) at the Medical Health and Research Institute, involving 60 women aged 20-40 years. The cohort consisted of 42 women diagnosed with endometriosis (study group) and 42 women undergoing IVF treatment without endometriosis (control group). Mitochondrial function, including ATP content and mitochondrial DNA (mtDNA) integrity, was assessed in oocytes retrieved from both groups. The study compared the outcomes of oocyte maturation, fertilization rates, embryo development, implantation rates, and clinical pregnancy between the two groups.*

Results: *The demographic and clinical characteristics of patients with endometriosis and controls revealed significant differences in age, body mass index (BMI), follicle-stimulating hormone (FSH) levels, and infertility duration. IVF outcomes showed no significant difference in clinical pregnancy rates (54.7% in endometriosis patients vs. 52.3% in controls), but endometriosis patients had slightly lower live birth rates (45.2% vs. 52.3%). Oocyte quality analysis indicated that endometriosis patients exhibited lower ATP content and mitochondrial number, particularly at the prophase I (PI) and metaphase I (MI) stages. Mitochondrial DNA deletions were found to have a significant negative impact on oocyte quality and IVF success, with all cycles involving oocytes with mtDNA deletions resulting in failure, including a biochemical pregnancy in a patient with moderate endometriosis.*

Conclusion: *Mitochondrial dysfunction, characterized by reduced ATP levels and mtDNA deletions, adversely impacts oocyte quality and IVF outcomes in women with endometriosis. These results highlight the importance of personalized IVF protocols that focus on mitochondrial health, potentially enhancing reproductive outcomes. Further research is needed to explore targeted interventions to minimize mitochondrial damage and improve ART success in this population.*

Keywords: Mitochondrial dysfunction, Assisted Reproductive Technologies, Endometriosis, Adenosine triphosphate.

Introduction: Endometriosis is a chronic, estrogen-dependent gynecological disorder defined by the ectopic presence of endometrial-like tissue outside the uterine cavity, typically involving the pelvic peritoneum, ovaries, and other extrauterine sites (Burney & Giudice, 2012; Zondervan et al., 2020). Approximately it affects an estimated 10% of women of reproductive age, is associated with infertility and poses challenges for assisted reproductive technologies, including in vitro fertilization (IVF). Endometriotic cells adapt to oxidative stress and hypoxia by altering their metabolic and cellular processes, enabling survival in these adverse conditions. Women with endometriosis often experience diminished fertility outcomes, including poor oocyte quality, impaired embryo development, and lower conception rates following assisted reproductive technologies (ART) such as in vitro fertilization (IVF).

These challenges are often attributed to the inflammatory environment, altered hormonal milieu, and ovarian dysfunction associated with endometriosis, all of which can negatively impact reproductive success (Latif S et al., 2023). The pathophysiological mechanisms underlying reduced fertility is complex and multifactorial, with emerging evidence implicating disrupted mitochondrial dysfunction plays a critical role.

Reproductive organs, like many tissues, have distinct metabolic and energy demands during development and adult function. (Torre SD et al., 2004). The mature oocyte, being the largest cell in the human body, contains a high number of mitochondria. The quantity and functionality of these mitochondria are crucial for the oocyte's development from primordial germ cells (Van Blerkom J. et al., 2011).

Mitochondria are integral for regulating key reproductive processes in females, such as oocyte maturation, fertilization, and early embryo development. Impaired mitochondrial function in oocytes from women with endometriosis can reduce energy production, elevate oxidative stress, and decrease embryo viability, ultimately lowering the chances of successful pregnancy. The Adenosine triphosphate (ATP) is generated through oxidative phosphorylation, a process that supplies the energy needed for critical cellular activities, including protein synthesis, DNA replication, and cell division (Assaf L et al., 2022). During oocyte maturation, fertilization, and embryo development, the high demand for ATP is critical to sustain cellular functions such as chromosome segregation, cytoskeletal reorganization, and the initiation of cell division. Mitochondrial dysfunction, characterized by decreased ATP synthesis, elevated reactive oxygen species (ROS) production, and damage to mitochondrial DNA (mtDNA), can directly impair oocyte and embryo quality, thereby diminishing the probability of a successful pregnancy (Kirillova A et al., 2021). Mitochondrial dysfunction has been extensively studied in relation to ovarian aging and metabolic stress (Demain LA, et al., 2017).

Endometriosis is linked to several pathophysiological alterations, including dysregulated inflammatory responses, hormonal imbalances, and increased oxidative stress, all of which can negatively impact mitochondrial function. These disrupted conditions may lead to mitochondrial damage, characterized by reduced ATP production, elevated oxidative stress, and cellular injury, all of which compromise oocyte quality and embryo development (Cecchino GN et al., 2018, Mate G, et al., 2018). Additionally, mitochondrial dysfunction can contribute to abnormal oocyte metabolism, impairing fertilization and early embryonic development, ultimately lowering the likelihood of a successful pregnancy following in vitro fertilization (IVF).

Several factors intrinsic to endometriosis may contribute to mitochondrial dysfunction. The presence of endometriotic lesions and the chronic inflammation associated with the condition can disrupt the balance between oxidative stress and antioxidant defense, leading to mitochondrial damage (Cacciottola L et al., 2021). Additionally, the hormonal dysregulation characteristic of endometriosis, particularly the imbalance between estrogen and progesterone levels, may adversely affect mitochondrial function and impair oocyte maturation. Current assisted reproductive technology (ART) strategies primarily concentrate

on optimizing ovarian stimulation protocols, embryo culture conditions, and genetic screening to enhance in vitro fertilization (IVF) success rates. However, these approaches do not specifically address mitochondrial dysfunction, which may play a critical role in improving oocyte and embryo quality in patients with endometriosis.

Emerging evidence indicates that embryo potential may be linked to the energy-generating capacity of oocyte mitochondria. By enhancing mitochondrial capacity, it may be possible to improve reproductive outcomes for women with endometriosis undergoing ART and provide new avenues for fertility preservation and treatment.

Methodology: This study is a prospective, hospital -based investigation designed to evaluate the impact of mitochondrial dysfunction on embryo quality and conception rates in women with endometriosis undergoing in vitro fertilization (IVF). The study will be conducted at the Medical Health and Research Institute over a period of three years, from December 2021 to December 2024. Ethical approval for the study was obtained from the institutional review board (IRB) of the Medical Health and Research Institute. All participants will be provided with written informed consent before enrollment.

Study Design: The study is a comparative cohort design, consisting of two groups: the study group, comprising women diagnosed with endometriosis, and the control group, consisting of women without endometriosis. The study will assess mitochondrial function in both groups, focusing on its role in oocyte quality, embryo development, and conception rates during IVF treatment. The inclusion criteria for participants in the study group include Women aged 20–40 years, Diagnosed with endometriosis confirmed through laparoscopy (diagnostic laparoscopy performed for clinical suspicion of endometriosis, Women undergoing IVF treatment, either for primary or secondary infertility. The inclusion criteria for the control group include: Women aged 20–40 years, No clinical or laparoscopy-confirmed evidence of endometriosis, Women undergoing IVF treatment for infertility due to other causes, such as male factor infertility, unexplained infertility, or tubal factor infertility.

A total of 84women will be enrolled in this study. Forty Two women diagnosed with endometriosis (study group) and Forty Two without endometriosis (control group) will be recruited. Participants will be selected from those attending the fertility clinic at the Medical Health and Research Institute.

In this study we have recorded the baseline assessment for demographic data -age, BMI, etc. and clinical characteristics, Laparoscopic Diagnosis of Endometriosis, IVF Protocol , Oocyte and Embryo Assessment and Embryo Implantation and Conception Rate.

Women suspected of having endometriosis will undergo diagnostic laparoscopy as a routine clinical procedure to detect endometriotic lesions. The severity of endometriosis will be categorized according to the American Society for Reproductive Medicine (ASRM) staging system (ASRM, 1997). Individuals diagnosed with endometriosis during the laparoscopy will be included in the study group.

IVF/ICSI protocol: Both participant groups will

undergo in vitro fertilization (IVF) treatment utilizing standardized ovarian stimulation protocols tailored to their individual ovarian reserve and response. Controlled ovarian stimulation (COS) will be achieved using recombinant follicle-stimulating hormone (rFSH) and/or human menopausal gonadotropin (hMG), in conjunction with a GnRH agonist or antagonist for ovarian suppression. Oocyte retrieval will be conducted under ultrasound guidance 36 hours following the administration of human chorionic gonadotropin (hCG).

Oocytes: Oocytes considered unsuitable for insemination or injection based on morphological assessment were selected for this study. These oocytes were at either the prophase I (PI) or metaphase I (MI) stage at the time of retrieval. The selected oocytes were cultured for 24–30 hours in P1 medium (Irvine Scientific) supplemented with 10% synthetic serum substitute, maintained under conditions of 5.5% CO2, 5% O2, and 90% N2. After the incubation period, the developmental stage of the oocytes was re-evaluated, followed by individual collection, lysis, and flash freezing in 100 µL of lysis buffer (Somatic Cell ATP Releasing Reagent; Sigma). The oocytes were subsequently stored at -80°C until further analysis.

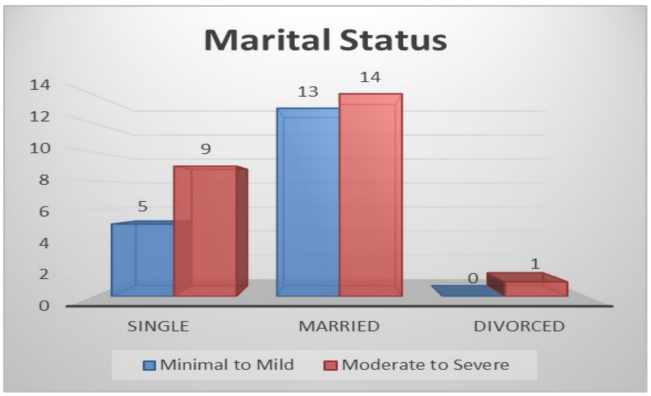
ATP Assay: The ATP content of individual oocytes was measured using a commercially available bioluminescent assay kit (ATP Bioluminescent Somatic Cell Assay Kit FL-ASC; Sigma), utilizing the luciferin-luciferase reaction. Reaction buffers were prepared in accordance with the manufacturer's instructions. A 100 µL volume of 1:5 diluted ATP assay mix was added to each well of a Costar white 96-well plate and incubated at room temperature for 3–5 minutes to allow endogenous ATP hydrolysis. In a separate tube, 100 µL of ice-cold somatic cell-releasing reagent, 50 µL of ultrapure water, and 50 µL of sample or standard were combined. A 100 µL aliquot of this mixture was transferred to a reaction well, and the emitted light was immediately measured using a luminometer (Dynex MLX Microtiter Plate Luminometer). Background luminescence was subtracted from all measurements. A 7-point standard curve was generated using final concentrations of 2.5, 5, 10, 25, 50, 100, 250, and 500 fmol/100 µL. The ATP content of the samples was then calculated based on the standard curve.

Statistical Analysis: Data entry was done using M.S. Excel and statistically analysed using Statistical package for social sciences (SPSS Version 16) for M.S Windows. Descriptive statistical analysis was carried out to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with n (%), while quantitative variables were summarized by mean ± S.D. All results were presented in tabular form and are also shown graphically using bar diagram or pie diagram as appropriate. The difference in the two groups was tested for Statistical Significance using Parametric tests such as t-test and categorical variables tested by chi square test. P-value <0.05 was considered statistically significant after assuming all the rules of statistical tests.

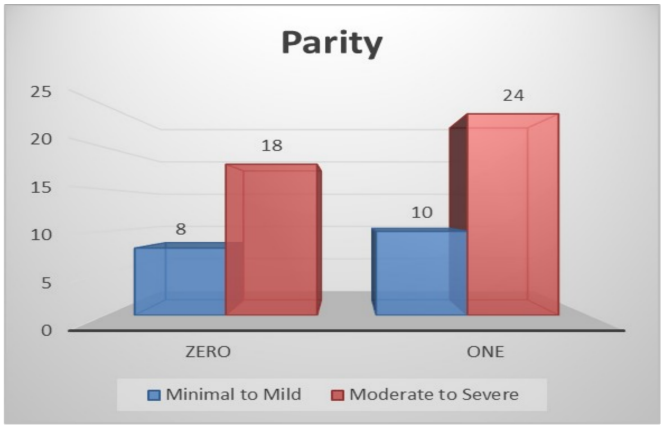
Results: This study assessed demographic and clinical parameters in individuals with surgically confirmed endometriosis and controls in the **Table 1**. Among patients with endometriosis, 18 had minimal to mild disease and 24 had moderate to severe disease and control were 42 patients. No significant differences in marital status, parity, or

infertility duration were observed between the two endometriosis subgroups (minimal to mild versus moderate to severe). The mean age for those with minimal to mild endometriosis was 24 ± 0.8 years, while those with moderate to severe disease had a mean age of 31 ± 0.6 years, compared to 32 ± 0.7 years in the control group. Body mass index (BMI) was slightly lower in the endometriosis group, with a median of 23.6 ± 0.7 for the minimal to mild group and 23.9 ± 0.2 for the moderate to severe group, in contrast to 25.9 ± 0.5 in controls. Follicle-stimulating hormone (FSH) levels were significantly lower in the endometriosis groups (7.19 ± 0.7 for minimal to mild and 7.49 ± 0.2 for moderate to severe) compared to controls (6.56 ± 0.4). In terms of marital status, most patients with endometriosis were married (13 out of 18 in the minimal to mild group and 14 out of 24 in the moderate to severe group), while 35 out of 42 controls were married and 6 were single(Depicted in Graph 1). Parity data indicated that 8 out of 18 women with minimal to mild endometriosis and 18 out of 24 women with moderate to severe disease were nulliparous(depicted in Graph 2). The mean duration of infertility was significantly longer in the endometriosis groups, with 6 ± 1.8 years in the minimal to mild group and 8 ± 1.8 years in the moderate to severe group, compared to 3.1 ± 0.6 years in controls. Primary infertility was more common in the moderate to severe endometriosis group (18 out of 24), while secondary infertility was 10 out 18 and 8 out of 24 distributed between the minimal to mild and moderate to severe endometriosis groups(Depicted in Graph 3). These findings highlight significant differences in age, BMI, FSH levels, marital status, parity, and infertility duration between the endometriosis and control groups.

Graph 1: Illustrates the Marital status of Women with Minimal to Mild and Moderate to Severe forms of Endometriosis



Graph 2: Illustrates the Parity of Women with Minimal to Mild and Moderate to Severe forms of Endometriosis



Graph 3: Illustrates the Infertility Condition of Women with Minimal to Mild and Moderate to Severe forms of Endometriosis

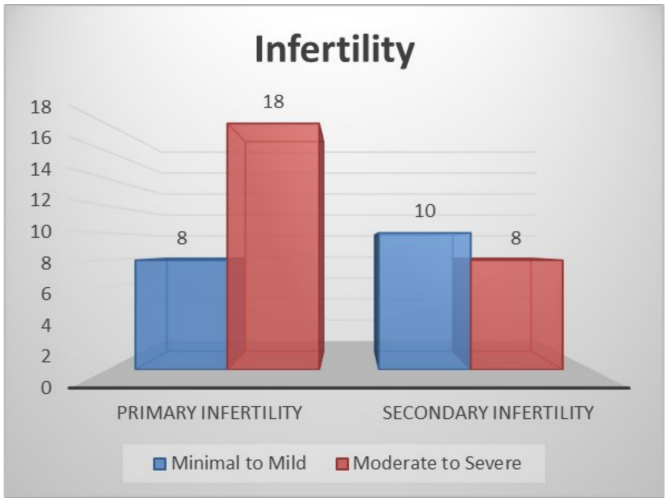


Table 1: Demographic factors and clinical outcome measures in individuals with surgically confirmed endometriosis and controls

Baseline Parameter	Surgical Endometriosis (n=42)		Controls (n=42)	P Value
	Minimal to Mild(18)	Moderate to Severe (24)		
Age (mean SEM)	24±0.8	31±0.6	32±0.7	0.001
BMI (median, [IQR])	23.6 ± 0.7	23.9± 0.2	25.9± 0.5	0.052
FSH (mean SEM)	7.19 ± 0.7	7.49 ± 0.2	6.56 ± 0.4	0.05
Marital Status				
Single	5	9	6	0.89
Married	13	14	35	
Divorced	0	1	1	
Parity				
0	8	18	36	0.86
1	10	24	6	
Duration of Infertility in years	6 ± 1.8	8 ± 1.8	3.1± 0.6	0.001
Primary Infertility	8	18	NA	0.18
Secondary Infertility	10	8	NA	
No of Subjects	18	24	42	

The Table 2 summarizes the characteristics of patients with surgically confirmed endometriosis, with ultrasound findings. The cohort consisted of 42 patients, including 18 with minimal to mild endometriosis and 24 with moderate to severe endometriosis. Among these, 26 patients were nulliparous. The average number of IVF cycles varied between 2 and 6. All patients were diagnosed with endometriosis through laparoscopy, with an average duration of 24 ± 0.8 years for the minimal to mild group and 31 ± 0.6 years for the moderate to severe group between the surgical diagnosis and IVF retrieval. Ultrasound examination showed that all patients had endometriomas, with an unspecified average size. Regarding the laterality of endometriomas, 29 patients had unilateral endometriomas, while 13 had bilateral endometriomas.

Table 2: Patients with endometriosis confirmed through surgical Diagnosis and Ultrasound Findings

Characteristics	
Total No. of Patients Minimal to Mild Moderate to Severe	**n=42** n=18 n=24
Nulliparous	26
Average IVF cycle no	2-6
No. of subjects with laparoscopic diagnosis of endometriosis	42
Average years between surgical diagnosis of endometriosis and IVF retrieval	24±0.6
No. of subjects with endometriomas on ultrasound	42
Average Size of Endometriomas	5-7cm
Laterality of Endometriomas Unilateral Bilateral	 29 13

In the **Table 3** there is a comparison of clinical outcomes between patients with surgically confirmed endometriosis (n=42) and controls (n=42), several parameters were evaluated. Endometriosis patients had slightly higher average AMH (3.1 ± 2.0 ng/mL) and antral follicle count (AFC) (8.9 ± 2.5) compared to controls (2.9 ± 1.8 ng/mL, 7.9 ± 2.7). Stimulation protocols varied, with higher gonadotropin doses (2504.18 IU) and longer stimulation durations (12 days) in the endometriosis group compared to controls (2214.37 IU, 10 days). Peak estradiol levels were similar between groups. Oocyte retrieval yielded more oocytes (11.00 vs. 9.00), and endometriosis patients had a higher mean percentage of mature (MII) oocytes (73.49% vs. 69.37%). Fertilization rates were also higher in endometriosis patients (69.06% vs. 67.04%). In embryo quality, the blastocyst formation rate was 72% in endometriosis vs. 76% in controls, and implantation rates were slightly higher in endometriosis (53.00% vs. 47.00%). Clinical pregnancy rates were comparable (54.7% vs. 52.3%), but the live birth rate was slightly lower in endometriosis patients (45.2% vs. 52.3%). These results suggest minor differences in ovarian response, oocyte quality, and IVF outcomes between endometriosis patients and controls.

Table 3: Clinical Outcome Measures Comparison between Subjects with Surgically Confirmed Endometriosis and Controls

Parameters	**Surgically Confirmed endometriosis (n=42)**	**Controls (n=42)**	**P-Value**
Ovarian Reserve and Stimulation			
Average AMH (ng/mL) (Range)	3.1 ± 2.0	2.9 ± 1.8	0.63
Average Antral Follicle Count (AFC) (Range)	8.9±2.5	7.9±2.7	0.08
Stimulation Protocol Used Short Long Antagonist	 19 16 7	 21 13 8	0.92
Total Gonadotropin Dose (IU)	2504.18 (2400.21–2608.15)	2214.37 (2142.08–2286.65)	
Duration of Stimulation (Days)	12	10	0.80
Peak Estradiol Levels (pg/mL)	506 (370–605)	489(374–598)	
Oocyte Retrieval and Fertilization			
Average No. of Oocytes Retrieved	11.00 [5–13]	9.00 [6–11]	
Average No. of Mature (MII) Oocytes	8.00(3-9)	7.00(2-8)	
Average No. of Mature (MI) Oocytes	2.00(1-3)	2.00(0-2)	
Mean percentage of mature (MII oocytes)	73.49%±5.68%	69.37%±4.37%	0.004
Fertilization Rate (%)	69.06%±2.44%	67.04%±3.97%	0.006
Embryo Quality			
Blastocyst Stage	72	76	
Average Number of Embryos Transferred	1	1	
Implantation rate (%)	53.00%(0-53%)	47.00%(0-47%)	
Clinical Pregnancy Rate (%)	23(54.7%)	22(52.3%)	1.00
Miscarriage Rate (%)	7(16.6%)	5(13.3%)	0.75
Live Birth Rate (%)	19(45.2%)	22(52.3%)	0.66

In the **Table 4** shows the distribution of oocytes at different maturational stages during retrieval in individuals with endometriosis (n=42) and controls (n=42). Of the total 26 oocytes at the prophase I (PI) stage, 12 were from the endometriosis group and 14 from controls. At the metaphase I (MI) stage, 14 oocytes were retrieved, with 6 from endometriosis patients and 8 from controls. The majority of oocytes were at the metaphase II (MII) stage, with 88 from the endometriosis group and 76 from controls, totaling 164 oocytes. Additionally, 13 degenerated oocytes were observed, 5 from the endometriosis group and 8 from controls.

Table 4: Distribution of oocytes across different maturational stages at the time of retrieval

Final stage	Stage at retrieval		Total
	Endometriosis (n=42)	Controls(n=42)	
PI	12	14	26
MI	6	8	14
MII	88	76	164
Degenerated	5	8	13

The ATP content and mitochondrial number in individual oocytes at various stages of maturation in endometriosis patients and controls undergoing IVF/ICSI is given in the **table 5** were Endometriosis Patients (n=42) and Control Patients (n=42).This data reflects the ATP content and mitochondrial number in oocytes at different maturation stages, comparing those from endometriosis patients and controls undergoing IVF/ICSI treatment were oocyte ATP content increases with maturation with the stage.

Table 5: ATP content and number of mitochondria in individual oocytes at various stages of maturation in endometriosis and controls undergoing IVF/ICSI

	Endometriosis Patients(n=42)			Control Patients(n=42)		
	PI	MI	MII	PI	MI	MII
ATP content (fmol)	736.2± 67.9	1,014.9±47.2	1,191.4±39.4	796.4± 77.9	1,122.9±44.9	1,304.4±34.4
No. of mitochondria (10^4)	6.5± 2.0	18.0± 4.4	14.3±3.1	8.5± 2.0	21.0± 4.4	17.3±3.1

P Value (PI):0.003

P Value (MI):0.001

P Value (MII):0.001

In the **table 6** outlines the characteristics of subjects and their oocytes with deleted mitochondrial DNA of the infertility treatment. The subjects, aged 26 to 33 years, exhibited FSH levels ranging from 7.12 to 7.56 U/L. Oocyte retrieval procedures resulted in 4 to 6 oocytes per individual, all successfully progressing to the metaphase II (MII) stage following in vitro maturation (IVM). Despite successful oocyte maturation, all cycles resulted in failure, including one biochemical pregnancy in a subject with

moderate endometriosis. These findings have the significant influence of mitochondrial DNA deletions on oocyte quality and IVF success rates, independent of the severity of endometriosis.

Table 6: Characteristics of subjects and oocytes with deleted mitochondrial DNA

Subject	Cause of infertility	Age (y)	FSH(U/L)	No. of oocytes retrieved	Final stage	IVM	Cycle Outcome
Subject 2	Minimal Endometriosis	26	7.12	6	MII	Yes	Failure
Subject 4	Mild Endometriosis	28	7.37	5	MII	Yes	Failure
Subject 9 Subject 10	Moderate Endometriosis	31	7.42	4	MII	Yes	Failure Biochemical
Subject 13	Severe Endometriosis	33	7.56	5	MII	Yes	Failure

Discussion: Studies indicate that endometriosis can impair mitochondrial activity, leading to oxidative stress, altered ATP production, and increased apoptosis, all of which can negatively affect oocyte competence and embryo viability. Mitochondrial dysfunction is significantly associated with poor embryo quality and lower conception rates in IVF patients with endometriosis.

Our study provides demographic parameters, including age and BMI, significantly differed between patients with endometriosis and controls. The endometriosis group showed a higher mean age compared to controls, particularly the moderate to severe subgroup, which is consistent with findings from previous studies that indicate endometriosis severity may correlate with increasing age due to disease progression over time (Giudice LC et al.2010), contributing to a delay in diagnosis and treatment (Giudice LC, et al., 2004). BMI in the endometriosis group, compared to controls, might reflect the impact of endometriosis on metabolism and body composition, although this difference was not clinically significant (Ferrero S et al., 2005). In contrast, the control group had a mean age of 32 ± 0.7 years, which is slightly older than the minimal to mild endometriosis group. The age differences between these groups are likely attributable to the progressive nature of endometriosis, which is often diagnosed in women after they have experienced symptoms for several years. Body mass index (BMI) was lower in the endometriosis groups compared to controls, which is consistent with findings from other studies that suggest women with endometriosis tend to have lower BMI compared to the general population (Jenabi E, et al., 2019). This observation may have clinical implications, particularly when considering lifestyle and dietary interventions for managing endometriosis.

Follicle-stimulating hormone (FSH) levels were observed to be significantly reduced in individuals with endometriosis, with levels reported as 7.19 ± 0.7 in the minimal-to-mild group and 7.49 ± 0.2 in the moderate-to-severe group, compared to 6.56 ± 0.4 in the control group. These findings are consistent with evidence suggesting that

endometriosis may adversely affect ovarian function and hormonal regulation as reported by (Chapron et al., 2019). Infertility duration was notably longer in minimal-to-mild (6 ± 1.8 years) and moderate-to-severe endometriosis (8 ± 1.8 years) compared to controls (3.1 ± 0.6 years). Primary infertility was most prevalent in the moderate to severe group (18 out of 24 patients), while secondary infertility showed a more balanced distribution between groups (10 out of 18 in the minimal to mild group and 8 out of 24 in the moderate to severe group). The high prevalence of primary infertility in the moderate-to-severe group (70%) underscores the significant reproductive impact of advanced endometriosis, consistent with prior research(Bhurke AV, et al., 2022).

Laparoscopy is the gold standard for the diagnosis of endometriosis, The majority of patients (62%) were nulliparous, consistent with the established link between endometriosis and infertility as reported by Somigliana et al. 2012. Ultrasound evaluations confirmed the presence of endometriomas in all patients, underscoring their high prevalence among individuals with endometriosis (Nisenblat V et al., 1996). In terms of laterality, 69% of patients presented with unilateral endometriomas, while 31% had bilateral lesions, consistent with evidence indicating unilateral dominance, though bilateral involvement is observed in advanced cases. Patients underwent an average of 2 to 6 IVF cycles, reflecting the significant reproductive challenges associated with endometriosis. Previous research has demonstrated that endometriomas can impair ovarian reserve, follicular development, and IVF outcomes (Somigliana et al., 2006). Nevertheless, advancements in assisted reproductive technologies continue to provide hope for women facing endometriosis-related infertility.

Patients with endometriosis required higher gonadotropin doses (2504.18 IU) and longer stimulation durations (12 days) compared to controls (2214.37 IU, 10 days), aligning with previous studies indicating reduced ovarian responsiveness in endometriosis (Uncu et al., 2013). Despite these variations, peak estradiol levels were comparable between the two groups, suggesting that controlled ovarian stimulation protocols can effectively promote follicular development.

Blastocyst formation rates were marginally lower in patients with endometriosis (72%) compared to controls (76%), while implantation rates were higher in the endometriosis group (53.0% vs. 47.0%). These results suggest that although embryo quality may be slightly compromised, the uterine environment remains receptive in endometriosis patients, consistent with studies indicating effective endometrial function following IVF (Macer & Taylor, 2012). Clinical pregnancy rates were similar between the groups (54.7% vs. 52.3%), though live birth rates were slightly lower in endometriosis patients (45.2% vs. 52.3%), consistent with previous research linking endometriosis to slightly reduced cumulative live birth rates after IVF (Hamdan et al., 2015). Endometriosis may present mild challenges in ovarian stimulation and embryo development; however, clinical outcomes, including pregnancy and live birth rates, are comparable to controls. These findings emphasize the need for personalized treatment strategies to optimize IVF outcomes in endometriosis patients, particularly those requiring higher gonadotropin doses or longer stimulation protocols.

Endometriosis patients exhibited a higher yield of mature oocytes (MII), the distribution of oocytes at different stages of maturation did not differ significantly from controls. This suggests that endometriosis may not severely impair oocyte maturation during controlled ovarian stimulation.

Endometriosis may slightly impact mitochondrial content and ATP levels in oocytes, but the general trend of increased ATP and mitochondria with oocyte maturation is maintained. This suggests that mitochondrial function and energy production are not significantly compromised during IVF/ICSI treatment in endometriosis patients, contrary to some reports of mitochondrial dysfunction (Hsu AL, et al., 2015). Mitochondrial DNA deletions have a significant impact on oocyte quality and IVF success rates, regardless of endometriosis severity. These findings emphasize the crucial role of mitochondrial function in oocyte maturation and fertilization, as mtDNA deletions impair energy production essential for successful embryo development (Wallace, 2010, Zhang D et al., 2017).

Conclusion: This study investigates key demographic, clinical, and IVF-related outcomes in women with endometriosis, with a focus on mitochondrial function's impact on oocyte quality and reproductive success. Endometriosis was associated with longer infertility duration, altered FSH levels, and increased gonadotropin requirements. However, IVF outcomes, including clinical pregnancy rates, were comparable to controls. While mitochondrial content and ATP levels in oocytes were mildly affected by endometriosis, oocyte maturation and fertilization capacity remained largely intact. Notably, mitochondrial DNA deletions were found to significantly impact oocyte quality and IVF success, emphasizing the essential role of mitochondrial function in reproductive outcomes. These findings highlight the need for personalized IVF protocols to address the specific challenges posed by endometriosis, aiming to optimize treatment outcomes and enhance reproductive health in affected women.

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Abbreviations: IVF, ATP,PI, MI,MII, mtDNA, ROS.

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