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Impact of Anti-Müllerian Hormone, Oxidative Stress and Lipid Profile Levels on Female Fertility

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ABSTRACT

Background: *Infertility also termed as a medical ailment of the reproductive system, hinders a person from conceiving. Anyone can develop this and its causes are many. Infertility is of three types: primary, secondary and unexplained. This blog will elaborate on the different types of infertility that stems from both males and females and try to unfold the complexities that come with this sensitive issue. Some common infertility causes include an irregular cycle of ovulation (the release of an egg on a monthly basis), low-quality semen, and blocked or damaged fallopian tubes.* ***Objectives***: *The plasma levels of anti-Müllerian hormone, oxidative stress, and lipid profile of women with reproductive issues will be examined in this study.* ***Materials and Methods***: *The case-control study included a total of 45 women who were healthy and 45 women who were unable to conceive World Health Organization. The study took place in the private clinic and the Babylon Teaching Hospital for Maternity and Children, which is located in Hilla City, and took place between the 1st of October 2023 to the 13th of December 2024. The enzyme-linked immunosorbent assay was used for the measurement of serum concentrations of the hormone whilst the SPSS software was used for the performing the statistical analysis.* ***Results***: *After conducting the research, it came to light that unlike the control group, patients in comparison had significantly diminished levels of the anti-miillerian hormone, while also displaying substantially elevated levels of oxidative stress and lipid profiles in the serum ($p < 0.05$).* ***Conclusion***: *The serum levels of the anti-miillerian hormone present in women suffering from infertility were lower than average, correlating with the high levels of oxidative stress. These findings indicate that oxidative stress is an important factor in most of the infertility pathogenesis mechanisms described in this manuscript.*

Keywords: Infertility, Ovulation dysfunction, ELISA, Pathogenesis, Reproductive.

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INTRODUCTION

Infertility as a painful medical condition to the reproductive system has drawn significant interest from researchers and clinicians alike. Griessler et al 2022 explained this condition as the inability to conceive which can be classified into primary, secondary, and unexplained types, each of which has its own unique set of causes. Engeli & Rothmayr Allison 2016 highlight that both men and women are affected by this condition, irrespective of their gen-der. A significant portion of infertility cases is attributed solely to the male factor (20 – 30%), female factor (20 - 35%), and both (25 - 40%). In a significant number of cases, the cause of the condition remains unknown between 10 – 20% (Chen et al 2019). Another key factor contributing to

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this problem, as noted by Jabir Edan et al 2023, is the age related decline in ovarian reserve, which is directly proportional to the production of anti–mullerian hormone. A dimeric glycoprotein AMH which belongs to transforming growth factor β superfamily, has a major role in the regulation of follicular development and ovarian function (Sova et al 2019).

Dewailly et al 2014 has underscored the significance of AMH as a marker for ovarian reserve assessment, predicting the ovarian response to stimulation, and treatment for various ovarian diseases. Beyond the hormonal factors, a growing body of literature indicates that oxidative stress and changes in the lipid profile may also be involved in the mechanisms of female infertility (Mozhgan Kohzadi and Mohammad Rasool Khazaei, 2020; Ruder et al, 2009). Oxidative stress is the result of the overproduction of reactive oxygen species and the failure of the body's antioxidant system to neutralize them, which has been correlated with poor oocyte quality, lower fertilization, and negative pregnancy outcomes (Vale-Fernandes et al, 2024). In addition, some studies have reported that abnormal circulating lipid levels may affect female reproductive processes possibly by altering hormone levels, steroidogenesis, and ovarian and uterine activity (Mahmood, 2009; Zhu et al, 2023). The present study seeks to assess the Association of lipid profile, oxidative stress, and anti-Mullerian hormone levels in women with developmental reproductive disorders and help to gain more information on the different aspects of contributors to female infertility.

METHODS

The study was investigated under the case-control framework with a total of ninety women from 18 to 44 years of age. One of the groups contained 45 infertile women, while the second group, referred to as the control group, contained 45 apparently healthy women. All the participants' body mass index was collected from women, both patients and controls, to improve the efficacy of the study. Simply put, the inclusion criteria centered around a patient group of women with diagnosed infertility and a control group of women of reproductive age without known health problems. To control for obesity, hypertension, thyroid problems, and any recent hormonal medication use, these parameters served as exclusion criteria.

The data was thoroughly checked and analyzed using appropriate standard measures. The data was expressed with the mean and the standard deviation, while the information was analyzed using the Student's t-test in combination with linear regression. To confirm the credibility of the results, SPSS (version 20) software was used and a p-value less than 0.05 was taken as statistically significant. Prior to conducting the work, the scientific committee of the Biochemistry Department at the Babylon Medical College reviewed and approved the study protocol. All respondents were debriefed on the purpose of the study and its proceedings, and they provided verbal consent for voluntary participation. Hence, the study was conducted in an ethical manner.

Human Anti-Müllerian hormone (Human AMH)

The Elabscience® Human AMH ELISA Kit is a fully integrated system intended for the quantitative determination of AMH concentration in human serum and plasma. The Sandwich-ELISA method is employed here with an HRP linked antibody and a pre-coated micro ELISA plate. The standard operational procedure of this kit involves sample (or standard) addition to the microplate followed by washing, substrate incubation, and measurement of color change which determines the AMH concentration. The kit contains all neccesary components and

reagents must be prepared and handled according to the instructions provided to achieve accurate and reliable results. The kit is for research purpose only and should not be used for diagnostic purposes.

Investigations (Biomarkers)

Apart from the level of anti-Müllerian hormone (AMH), the study also assessed the concentration of lipid profile markers, oxidative stress markers, and the antioxidant capacity of the serum of the participants. Lipid profile analysis involved the evaluation of high-density lipoprotein (HDL) cholesterol, triglycerides (TG), low-density lipoprotein (LDL) cholesterol and total cholesterol (TC). For the evaluation of oxidative stress, serum levels of MDA, which is a biomarker for lipid peroxidation, were measured. The assessment of antioxidant status was based on the measurement of total antioxidant capacity and the activity of superoxide dismutase (SOD) in the serum samples. All of these additional analyses were done in compliance with the established methods and procedures in order to ensure a global evaluation of the metabolic and oxidative parameters of the study population. After these investigations, the results were measured against the AMH levels which enabled a better insight into the cross relations between hormonal, lipid, and oxidative activity in the context of female fertility.

RESULTS

Table 1 gives a detailed comparison of the biochemical parameters of the control group as well as the patient group. The data also shows that the mean age for the patient group was 36.7 ± 3.4 years versus the control group, which was 32.5 ± 4.2 years. The similar age ranges between the two groups assist in making a just comparison. In regards to body mass index (BMI), the patient group had a primary mean BMI of 27.2 ± 2.1, which is greater than the 25.3 ± 1.7 mean in the control group. This difference, although statistically insignificant ($p > 0.05$), indicates that the infertile women might have had an inclination for overweight. The key variable of interest, the anti-Müllerian hormone (AMH) levels, showed a stark contrast between the groups. The patient group had an average AMH concentration of 1.31 ± 0.7 ng/mL which was significantly lower ($p < 0.05$) than the 2.82 ± 0.63 ng/mL average of the control group. This finding correlates with the expectation that women in the patient group suffer from infertility due to diminished ovarian reserve, which is apparent from reduced AMH levels.

Considering the lipid profile parameters, the infertile patients had significantly lower HDL cholesterol (37.2 ± 4.2 mg / dL vs. 45.1 ± 4.8 mg / dL, $p < 0.05$) and more elevated triglycerides (175.2 ± 13.3 mg / dL vs. 134.3 ± 15.7 mg / dL, $p < 0.05$), LDL cholesterol (135.7 ± 15.9 mg / dL vs. 112.2 ± 17.3 mg / dL, $p < 0.05$), and total cholesterol (198.5 ± 11.2 mg / dL vs. 155.3 ± 10.7 mg / dL, $p < 0.05$) as compared to the study group. There was a difference worth noting in the fact that some parameters of oxidative stress, malondialdehyde (MDA), and some of the total antioxidant capacity and superoxide dismutase (SOD) activity as the markers of the antioxidant defense system did not change statistically significant between the two groups ($p > 0.05$)., In this particular case, the information captured in the table is necessary to understand the altered biochemical profile in women with infertility as compared to normal women and the possible relations between diminished reserve of ovaries, dysfunctional lipid metabolism, and female infertility.

Table 1. Biochemical characteristics of the control and study population.

Variables	Group	No	Mean ± SD	95% confidence interval for Mean		Sig. value
				Min	Max	
Age (years)	Patients	45	36.7 ± 3.4	33.3	40.1	p > 0.05
	Control	45	32.5 ± 4.2	28.3	36.7	
Body mass index (BMI)	Patients	45	27.2 ±2.1	25.1	29.3	P > 0.05
	Control	45	25.3±1.7	23.6	27.5	
Anti-Mullerian hormone (AMH) ng/mL	Patients	45	1.31±0.7	0.61	2.21	p < 0.05
	Control	45	2.82±0.63	2.19	3.75	
HDL cholesterol (mg/dL)	Patients	45	37.2±4.2	33.1	41.4	p < 0.05
	Control	45	45.1±4.8	40.3	49.9	
TG (mg/dL)	Patients	45	175.2±13.3	161.8	189.5	p < 0.05
	Control	45	134.3± 15.7	118.6	150.1	
LDL cholesterol (mg/dL)	Patients	45	135.7± 15.9	120.6	150.8	p < 0.05
	Control	45	112.2±17.3	94.9	129.5	
Total cholesterol (mg/dL)	Patient	45	198.5±11.2	187.3	209.7	p < 0.05
	Control	45	155.3±10.7	144.6	166.8	
Very-low-density lipoprotein (mg/dL)	Patients	45	41.2 ± 4.2	37.2	45.4	p < 0.05
	Control	45	22.1±3.9	18.2	26.7	
MDA (nmol/ml)	Patients Control	45	148.3±20.1	128.2	168.4	p > 0.05
Total antioxidant (U/ml)	Patients Control	45	11.7 ±1.2 12.3 ± 2.3	10.5 10.1	12.9 14.6	p > 0.05
SOD U/ml	Patients Control	45	45.2±5.3 44.9±6.9	39.9 38.2	50.5 51.6	p > 0.05

significant = P< 0.05

The correlations of biochemical variables from the study are summarized in Table 2. Considering the correlations with AMH levels, a substantial positive correlation was observed between the AMH level and SOD activity (r = 0.689, p <0.05), suggesting that women with health ovaries (higher AMH) tend to have relatively strong antioxidant defense systems, which are expected to assist in protecting oocytes and reproductive functions.

AMH levels on the other hand showed a strong negative correlation with several of the lipid profile parameters such as triglycerides with (r=−0.571, p<0.05), LDL-C (r=−0.532, p<0.05), and total cholesterol (r=−0.602, p<0.05). Such a correlation suggests that diminished ovarian reserve

indicated by lower AMH levels may go hand in hand with an increased level of unfavorable lipid which can increase health risks. Using data from Table 2 and correlation analysis reveals the positive association between some other cardiovascular apple's indices, which include malondialdehyde (MDA) triglycerides ($r = 0.489$, $p < 0.05$) and total cholesterol ($r = 0.479$, $p < 0.05$). It points in the direction that there is considerable increased lipid peroxidation as indicated by higher MDA levels and adverse lipid profile in these women.

It is important to note, that total antioxidant capacity revealed a significant adverse correlation with triglycerides ($r = -0.604$, $p < 0.05$) and total cholesterol ($r = -0.597$, $p < 0.05$). This implies that weakened changes on cholesterol levels and increased total triglycerides may worsen arsenal. Such correlation analyses are instrumental in knowing how exactly these systems that is hormonal, lipid, and oxidative stress parameters interact with one another which emphasizes the complex details of the potential causes of female infertility. These mechanisms are correlated and thus undergoing meticulouse separation helps for better systematic intentions and management plans for women having reproductive problems.

Table 2: Correlation between the measured parameter sequence variables beside each other.

Sequence	Variables against each other	Correlation (r)	Sig. value
1-	AMH vs T Cholesterol	-0.78	$p < 0.05$
2-	AMH vs TG	- 0.53	$p < 0.05$
3-	AMH vs HDL	0.91	$p < 0.05$
4-	AMH vs LDL	-0.65	$p < 0.05$
5-	AMH vs VLDL	-0.78	$p < 0.05$
6-	AMH vs MDA	-0.59	$p < 0.05$
7-	AMH vs T antioxidant	0.82	$p < 0.05$
8-	AMH vs SOD	-0.41	$p < 0.05$

DISCUSSION

This deep investigation contributes to a better understanding of the complex interplays between anti-Müllerian hormone (AMH) and lipid profile changes and oxidative stress parameters in relation to women infertility. The findings bring new information that add deeper comprehension about complex physiology of reproductive health. There are available data to support the claim that levels of AMH in the infertile patient group were significantly lower than in the healthy control group. The decreased level of AMH concentration is a common finding in the evaluation of Diminished Ovarian Reserve and is clearly accepted as one of the most important causes of female infertility [(Smith et al. 2015);(Lee et al., 2018)]. AMH is accepted as an objective clinical and biochemical marker for estimation of the functional ovarian reserve, and its decrease is attributed to aging and other pathological conditions of the ovaries [(Broer et al., 2014); (Tal et al., 2020)].

What was surprising about the current study was that some differences in the lipid profiles of the two groups that were compared could be seen. First, the infertile patients had a less favorable lipid profile denoted by lower HDL cholesterol, increased levels of triglycerides, LDL cholesterol, and total cholesterol in comparison to the healthy controls (*Al-Ziaydi AG., 2024)*. These findings are in agreement with earlier studies that have reported the association between dyslipidemia and impaired fertility in women [(Williams et

al., 2011);(Mulukutla et al., 2016)]. It is possible that the altered lipid metabolism contributes to the reproductive pathology, particularly the polycystic ovarian syndrome (PCOS), which is one of the most common factors responsible for female infertility [Escobar-Morreale and Luque-Ramírez (2013)]. The negative correlations observed between AMH and the lipid profile parameters suggest that there is a connection between lowered ovarian reserve and adverse lipid profile. This link, however, seems to be multifactorial, entrenched in hormonal and metabolic interactions in which the finely tuned interplay between reproductive hormones and lipid metabolism is disturbed and may therefore have harmful consequences on fertility [(Robker et al., 2009);(Valckx et al., 2012)].

The study revealed missing statistically quantifiable variation between both groups in malondialdehyde (MDA) levels as well as the antioxidant network deficiency. This finding is somewhat unexpected as past research has implied a steady increase in oxidative stress and diminished antioxidant defense in individuals experiencing infertility Olusina Depanise et al. However, the positive correlation existing between AMH and superoxide dismutase (SOD) activity as noted in the study signifies that strengthening the antioxidant system may be vital in sustaining ovarian activity as well as fertility. One possible limitation of the analyzed study is the existence of few subjects which goes against the study finding recruitment of a larger cohort population in order to achieve more accurate results. In addition, the cross-sectional nature of the study design does not allow for the determination of cause and effect relationships, and these variables would be much clearer after longitudinal studies have been done. To sum up, the current study indicates the potential interplay between reduced reproductive capacity, as measured with AMH, altered lipid metabolism, and possible antioxidant protection in women who experience infertility. Comprehensive evaluation of hormonal, metabolic, and oxidative changes is critical in the understanding the assessment and the treatment, if needed, of reproductive health issues. More extensive research with a greater focus on the technologies and methods of population reproduction is likely to provide better insight into the mechanisms of these processes and help to formulate appropriate and effective ways to solve the problem of preserving and restoring reproductive function in women (Sahin et al., 2019).

CONCLUSION

Through this research, we have revealed profound interrelationships between a woman's reproductive health, her metabolic profile, and her body's ability to cope with oxidative stress. The challenges of infertility among women are truly sophisticated as depicted in some of the key findings.

Considerable differences in the levels of an anti-Müllerian hormone (AMH) between the healthy and infertile groups confirm the critical role of low ovarian reserve in reproductive barrenness problems. This decrease in a critical fertility biomarker points to the necessity of close monitoring and early remedial actions to enhance a woman's reproductive potential. The study covered troubling discrepancies in the lipid profiles of the two groups studied. Alongside the hormonal imbalances, the infertile women displayed an unfavorable pattern of higher triglycerides, LDL cholesterol, and total cholesterol while HDL cholesterol was lower. This negative metabolic status could result in reproductive complications which amplify the need to address these imbalances.

The negative correlations between AMH and the problematic lipid parameters point toward the need to disentangle the

relation between hormonal and lipid metabolism factors. It is possible that abnormalities within a certain range may be beneficial while significant disruption of the balance may have detrimental effects on a woman's fertility. The study did not locate distinct differences in oxidative stress markers, but the positive association between the antioxidant enzyme superoxide dismutase (SOD) and AMH demonstrates the protective barriers that a strong antioxidant system could serve in preserving the ovarian function and fertility. Weaknesses of this study include the limited number of participants and cross-sectional methodology, which advocates for more comprehensive studies with greater populations and longitudinal methods. This information may assist in designing specific measures such as targeted dieting, lifestyle changes, and medicating to improve the reproductive health of women with infertility issues (Sahin et al., 2019).

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Conflicts of interest:

The authors declare that they have no competing interests and no conflicts of interest in the current study.

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