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Original Research Article

Positive correlation between latent female genital tuberculosis and low anti-mullerian hormone levels in young individuals

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ABSTRACT

Background: The female vaginal tract is likely getting more like to be latently affected by tuberculosis today. By using typical tests like animal vaccinations, culture, and histology, this participation is challenging to diagnose. Some researchers have investigated the tubercular disease's ovarian affliction bacteria, but further research is needed on hormonal affection. In those circumstances, evaluating anti-Mullerian hormone (AMH) is used to gauge how well the ovaries are functioning.
Methods: 200 patients who visited Janm IVF Centre, Bhagalpur within a year with clinically relevant indications verified infertility were intended for in vitro fertilization. 180 of these individuals who met the criteria for inclusion were recommended to have a PCR (polymerase chain reaction) and as a standard examination of their ovarian function to estimate the hormone test. A control group of 105 fertile individuals was also included.
Results: Out of the 180 subjects, 50 (44.46%) were not detected by PCR, while 130 (55.54%) were. A statistically significant difference has been found between the AMH levels in the PCR-positive group and the PCR-negative and fertile group.
Conclusions: Infertility can result from tubercular involvement of the reproductive tract because it reduces AMH secretion and ovarian reserve.

Keywords: Anti-Mullerian hormone, Genital tuberculosis, In vitro fertilization, Ovarian reserve test, Polymerase chain reaction

INTRODUCTION

According to statistics available, the approximate occurrence of female genital tract tuberculosis (FGTB) in wealthy nations like the USA is 1%, compared to 17% in India.[1] Based on immunological status in certain infected individuals, TB bacillus initially enters the body via way of the lungs and remains dormant without causing any clinical symptoms. As of right now, there is a dearth of trustworthy confirmatory tests for this quiet variant.[2] Latent genital tuberculosis (LGTB) or genital tubercular infestation (GTBI) are the terms used to describe this. This may result in ovulatory disorders due to ovarian involvement, poor implantation due to tubal obstruction, infertility due to ovarian involvement, poor implantation due to endometrial involvement, as shown in Figure 1. The majority of a woman's reproductive capacity, regardless of her chronologic age, may be anticipated by her ovarian reserve, which establishes the pharmacologic age of the ovary.

The amount of prehistoric ovarian follicles that each woman has at birth is constant, and it decreases annually until menopause, at which point only fewer than ten follicles are left. An inadequate ovarian reserve, which directly affects the calibre of oocytes, is eventually caused by this normal decline as measured by the number of primordial follicles.[3] Although the mechanisms governing ovarian ageing are yet unknown, women with low ovarian reserves are reported to have poor ovarian stimulation

responsiveness. On days 2 or 3 of a natural cycle, infertile women are said to have weak ovarian reserves if their levels of the hormones follicle stimulating hormone (FSH) and anti-Müllerian hormone are high and low, respectively. To forecast ovarian response, hormonal signals are employed.

Hormonal indicators are used to predict ovarian response. On ultrasound, ovarian blood flow and a low antral follicle count (AFC) are also seen as indicators of reproductive potential. As a result, AMH ovarian response and female reproductive potential are accurately predicted by this factor.[4] AMH secretion in humans reaches its peak several years following puberty, followed by and then declines with ageing, becoming nearly during menopause, undetectable, and probably reflecting the ageing-related loss of ovarian reserve. Low AMH levels are found while evaluating the ovarian reserve in LGTB or GTBI patients, especially prior to IVF.

Hysteroscopy and laparoscopy can occasionally show tubal and endometrial involvement of the tubal and endometrium, but nothing is known regarding ovarian involvement. The poor outcomes specifically in the response to the intrauterine ovulation induction a cycle of insemination or IVF, might be caused by Mycobacterium TB's impact of toxicity on ovarian reserve.[5] A tissue-based smear culture, an epithelioid granuloma on histopathology, or the discovery of acid-fast bacilli (AFB) from a laparoscopy can all be used to confirm an unequivocal diagnosis of LGTB instead of an HSG or laparoscopy.[6]

Histopathology and tissue-based culture are occasionally insufficiently sensitive because of the decreased bacterial burden.[7] There is evidence in the literature that PCR technology can be used to diagnose LGTB.[8,9] Such tests also have the best possible efficiency.[10,11] Ovarian function, particularly the endocrinological reserve, is impacted in even when there is no direct ovarian involvement in latent TB patients.[12,13]

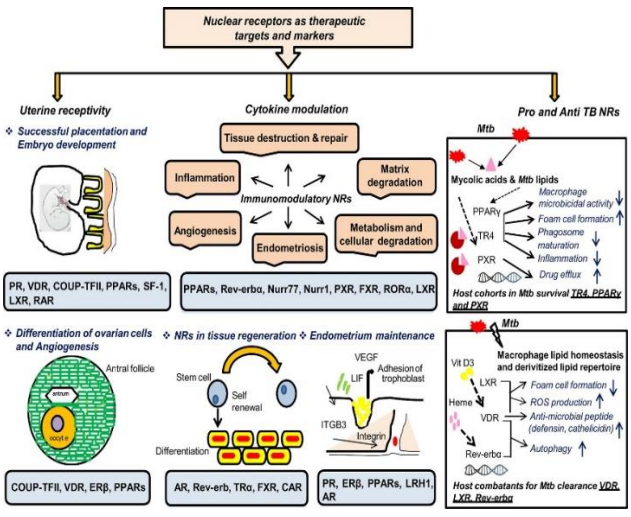

Figure 1: Etiopathogenesis of female genital tuberculosis.[14]

METHODS

Study design

This was a prospective study carried out at Janm IVF Centre, Bhagalpur from October 2021 to November 2022.

Methodology

In two successive cycles, the chosen patients underwent PCR tests on both the menstrual blood and endometrial aspirate, both PCR results (positive and negative) were acceptable results among all samples used in this study. The study included those whose PCR results were both positive and negative across all sample sets. 105 fertile subjects who met the criteria for inclusion served as a fertile control group for the same length of follow-up. Since they were born within six months of the counselling, PCR tests were not run on these patients. To assess ovarian function, the AMH levels were compared between TBPCR positive and negative cases as well as to a fertile control group.

The chosen patients underwent 2 consecutive cycles of PCR testing on both the endometrial aspirate and menstrual blood. All samples included in this investigation had both positive and negative PCR results. The study included those whose PCR results in all samples were both positive and negative. During the same follow-up time, 105 fertile participants who met the inclusion criteria served as the control group. These patients' PCR tests were not run because they had given birth within 5 months after receiving counselling. The AMH levels in TBPCR positive and negative patients, as well as in comparison to a fertile control group, were examined to evaluate ovarian function.

Based on each subject's hormone condition, a counselling approach was used to begin medication before ovulation induction. By using the strategy, 105 participants were conceived within 5 months after the treatment began and were treated as the normal control group.

MH levels are determined using the AMH Gen II ELISA. The serum samples for the AMH Gen II Elisa were incubated with calibrators and controlled at room temperature in microtiter wells coated with anti-AMH antibodies. A 2-site immunoassay that has been enzymatically amplified is what this process is called. To measure the substrate's enzymatic turnover, which is clearly connected to the amount of AMH in the blood, anti-AMH detection antibody, enzyme, and substrate are sequentially incubated and washed.

Sample Size

200 patients originally enrolled for this study, based on the inclusion criteria, 180 patients were finalized for this study.

Inclusion criteria

The participants included in the research had to be between the ages of 25 and 41, have regular periods, be free of hyperprolactinemia, hypothyroidism, or hyperandrogenism, and have FSH values less than 11 µ/ml and luteinizing hormone (LH) values less than 11 µ/ml earliest stage of the follicle. These individuals' transvaginal ultrasounds (TVS) and clinical assessments found no pelvic pathology.

Exclusion criteria

Polycystic ovarian syndrome patients and those with a history of taking anti-tubercular drugs (ATD) in the past or present were excluded from the study.

Statistical analysis

The mean, median, lowest, and highest AMH concentrations were shown using histograms and the interquartile range formula (IQR) in the PCR positive and negative as well as fertile control groups. A non-parametric Mann-Whitney test was conducted on the AMH value of the first three groups to ascertain the variation in population averages. To determine the concentration of AMH groups in the sample, a nested ANOVA was used. In our study, the AMH concentration had a sensitivity and specificity of 36.2% and 96.0%, respectively, for the diagnosis of pregnancy. The AMH concentration has a positive predictive value for diagnosing pregnancy of 90.6% and a negative predictive value of 58.5%. All statistical analysis was done in MINITAB 17.

Ethical consideration

The study was approved by the ethical committee of Rahman Nursing Home, Bhagalpur after written consent was obtained from the subjects.

RESULTS

The average body mass index was 24.31 kg/m^2 for the former group compared to 22.78 kg/m^2 for the latter group, and the average menstrual cycle length was 31.13 days compared to 29.67 days, respectively, for all infertile subjects undergoing IVF and those of the normal fertile group (Table 1).

Table 1: Patterns of infertility and normal in the population.

Traits	Infertile		Fertile	
	Mean	Range	Mean	Range
Age in years	30.25	21-38	28.26	23-37
Typical cycle (days)	31.13	24-34	29.67	24-34
Body mass index (kg/m^2)	24.31	17.3-31.4	22.78	17.3-31.4

Table 2: AMH concentration descriptive statistics using the IQR formula (interquartile range).

Criteria	Mean	Median	Min	Max	IQR
Fertile group (n=105)	5.695	5.090	1.150	15.260	3.037
PCR negative (n=50, 44.46%)	6.431	5.3	1.880	22.750	4.525
PCR positive (n=130, 55.56%)	0.863	0.780	0.010	0.780	0.790

Table 3: AMH concentration and value expressed as a percentage and the 95% confidence interval.

Age (years)	Normal control group	Infertile		A P-value of Mann-Whitney test		
	AMH median concentration in percent with 95% confidence interval	AMH median concentration in percent with 95% confidence interval		Infertile PCR positive - normal	Infertile PCR negative - infertile PCR positive	Infertile PCR negative - normal
		PCR negative	PCR positive			
20-25	658.0 (577-969)	465.5 (210-771)	113.0 (90.5-133)	0.001	0.001	0.514
26-30	629.0 (458-789)	535.0 (478-791)	114.5 (83.5-151)			
31-35	412.5 (349-537)	645.5 (542-803)	99.0 (81.5-118.5)			
36-40	490.0 (389-619)	374.0 (276-549)	64.0 (42.5-75.5)			

50 (44.46%) participants were PCR negative, while 130 (55.54%) subjects had DNA PCR positive results from both menstrual blood and endometrial aspirate (Table 2). PCR wasn't carried out on any of the 105 subjects.

The PCR-positive group's AMH concentration was discovered to be considerably lower than that of the PCR-negative and fertile group. The median AMH levels in PCR-negative individuals were almost identical to that of fertile subjects (Table 2).

In Table 3, the age-stratified distribution of AMH concentration showed that it was significantly lower in the PCR-positive group compared to the PCR negative group and the fertile group.

Table 4: Percentage of patients by age in the fertile, PCR-positive, and PCR-negative groups.

Age (years)	Fertile group	Infertile	
	Percentage of patients	Percentage of patients	
		PCR-negative	PCR - positive
20-25	16	10	3
26-30	38	32	17
31-35	32	42	41
36-40	10	12	35

Table 4 lists the age-specific patient percentages for the PCR positive group, PCR negative group, and fertile group.

DISCUSSION

Latent tubercular infection is gaining importance because of its major impact on the reproductive system. The simple presence of bacilli and damaging cytokine release by GTBI cause its negative effects.[9] The ovaries may also be affected by a similar process, as low AMH might be a sign indicating decreased ovarian activity caused by damaging inflammatory cytokines. Most women experience retrograde menstruation as a common occurrence. This blood might flow into touch with the ovary in PCR-positive patients, thereby impacting the negative effects of inflammatory cytokines.[10]

This study demonstrated that AMH levels were significantly lower in those with genital tract tuberculosis or in the TB-PCR-positive group. AMH levels are frequently used to assess the early follicular FSH, antral follicular FSH, and ovarian reserve, which regulate the ovulatory process.[11] AMH is stable throughout the cycle with little change in the follicular or luteal phases. Low AMH levels alter the ovary's behaviour during folliculogenesis, which eventually becomes a sign of ovulatory failure in those with positive TB-PCR tests.[12] The juxtaposition of the AMH level in PCR is positive and negative cases likewise revealed a significant difference, even after age-stratified results were taken into account.

In afflicted patients, an ovarian reserve decline that is statistically significant was discovered. Estimated levels of AMH in the fertile controls were found to be significantly higher than those in the infertile group, but significantly lower than those in the TBPCR positive and marginally greater than those in the TBPCR negative cases. In this investigation, the AMH level was estimated following antitubercular therapy completion. Despite being 14% higher than the prior measurement, the AMH level did not increase by more than 24%. The fact that this increase was not age-specific is intriguing.[13]

The level of AHM was estimated at two and five months integrated into therapy. After several 5 months of the medication, the AMH value increased from the value after 2 months. Since oestrogen reserve in proportion to AMH level defines a woman's fertility potential, participation of latent tuberculosis causes harmful effects. on a woman's capacity to procreate.

The small sample size was one of the elements for limitations of this research. One cannot speak of the long-term effects of genital TB. A prospective multi-institution study that included multiple institutions could allow for a direct comparison of management strategies and outcomes while also removing the single-institution bias.

CONCLUSION

Tuberculosis in the genitalia of humans decreases the capacity to reproduce in addition to negatively impacting fallopian tubes pr uterus. Reduced AMH levels in persons who are afflicted serve as evidence of this.

Recommendations

Women having IVF who have genital tract tuberculosis exhibit a poor ovulatory response to stimulation. This is most likely caused by weakened ovarian function, as seen by a decline in AMH level.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of Rahman Nursing Home, Bhagalpur

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