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Article

Hormonal, Immunological, and Familial Risk Factors Influencing Pregnancy Outcome after Intrauterine Insemination in Tikrit, Iraq

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Abstract: Background: Infertility affects roughly 15% of couples globally with female-factor infertility contributing to nearly 40% of the cases. Intrauterine insemination (IUI) is the first line assisted reproductive technology (ART). The outcome depends largely on the relationship between the hormonal environment and immunological tolerance at the endometrial interface. **Objectives:** The purpose of this study is to assess certain biochemical hormones and immunological markers in women receiving intrauterine insemination (IVI) in Tikrit, including follicle stimulating hormone (TSH), prolactin, estrogen, testosterone, and ANA. We will also look for correlations with pregnancy rate, BMI, and family genetic history. **Methods:** One hundred women who were having intrauterine inseminations (IUIs) at the Reproductive Medicine Unit of Tikrit Teaching Hospital were the subjects of a prospective case-control study that ran from September 2023 to April 2024. A total of 47 pregnant women and 53 non-pregnant women made up the study's participants. During the second and third days of menstruation, blood samples were taken. The chemiluminescent immunoassay and enzyme-linked immunosorbent assay were used to conduct the hormonal tests. We used a multiplex bead-based immunoassay to profile cytokines. Using a standardized questionnaire, we were able to determine body mass index and document family history. In addition, the discriminative performance of important biomarkers was assessed using receiver operating characteristic (ROC) analysis. **Results:** While the pregnant group showed noticeably increased levels of AMH, E2, IL-10, IL-4, and CD4+/CD8+ ratio, the non-pregnant group showed considerably enhanced levels of FSH, prolactin, TSH, testosterone, IL-6, TNF-α, NK cell activity, anti-sperm IgG, ANA titers, antiphospholipid antibodies, and CRP ($p<0.05$). BMI was positively correlated with pro-inflammatory cytokines and significantly negatively correlated with pregnancy rate and AMH levels ($r=-0.48$, $p<0.001$ and $r=-0.52$, $p<0.001$, respectively). Pregnancy probabilities were considerably lowered ($p<0.05$) in cases where there was a positive family history of infertility, polycystic ovary syndrome, autoimmune disease, or thyroid condition. An AUC of 0.99 was achieved for the discriminative performance of a combined biomarker model for pregnancy outcome, which included AMH, BMI, IL-6, IL-10, and FSH. **Conclusions:** The hormonal and immunological profile is a robust predictor of IUI outcome. Elevated BMI and positive family genetic history independently reduce

pregnancy rates, underscoring the need for personalized pre-IUI assessment integrating metabolic, immunological, and genomic risk stratification.

Keywords: Artificial insemination; intrauterine insemination; infertility; cytokines; AMH; anti-sperm antibodies; BMI; family history; immunological markers; ROC analysis; Tikrit.

Introduction

Infertility, characterized as the inability to attain a clinical pregnancy following 12 months or more of consistent unprotected sexual activity, impacts approximately 48.5 million couples worldwide [1,2]. In Iraq, prevalence statistics indicate rates that are similar to or surpass worldwide averages, affected by consanguineous marital customs and restricted access to early reproductive services [3]. Intrauterine insemination (IUI) involves the direct placement of processed sperm into the uterine cavity and is recognized as the least invasive and most economical form of assisted reproductive technology (ART), exhibiting cumulative pregnancy rates ranging from 20% to 60% based on factors such as etiology, ovarian stimulation methods, and patient criteria [4,5].

The endometrium is not merely a passive entity; implantation necessitates a highly orchestrated immunological interaction between the semi-allogeneic embryo and the maternal decidua. This conversation is coordinated by a system of pro-inflammatory and anti-inflammatory cytokines, uterine natural killer (uNK) cells, regulatory T-cells, and antigen-presenting cells. Dysfunction within this immunological network—evidenced by heightened peripheral natural killer (NK) cell cytotoxicity, autoantibody synthesis, or an imbalanced Th1/Th2 cytokine profile—is progressively acknowledged as a contributor to unexplained infertility and implantation failure [6].

Simultaneously, biochemical indicators such as anti-Müllerian hormone (AMH) representing ovarian reserve, follicle-stimulating hormone (FSH) reflecting ovarian response, and androgens like testosterone serving as proxies for polycystic ovarian syndrome (PCOS) collectively outline the hormonal framework influencing IUI success [7,8]. Recent findings suggest that body mass index (BMI) serves as an autonomous regulator of hormonal systems and inflammatory processes: adipose tissue acts as an endocrine organ, releasing adipokines that exacerbate systemic inflammation and hinder ovarian follicle development [9].

Genetic inclination adds complexity to the clinical scenario. A familial history of infertility, PCOS, endometriosis, or autoimmune disorders increases individual risk, probably due to common genetic variations in immune-regulatory genes (e.g., FOXP3, HLA-DQ, MTHFR) [10]. This aspect is yet inadequately defined in Middle Eastern populations, where inbreeding can enhance the genotype-to-phenotype expression [11].

This study aimed to offer a full biochemical and immunological profile of Iraqi women receiving IUI in Tikrit, and to explain the predictors of pregnancy result including BMI stratification and family genetic history. Based on the above, the present study was intended for achieving the following precise objectives:

- To assess and compare selected reproductive hormones (FSH, LH, AMH, E2, progesterone, prolactin, TSH, testosterone) between women who conceived following IUI and those who did not [12].
- To compare and quantify selected immunological markers (IL-6, IL-10, IL-4, TNF-?, NK cell activity, anti-sperm antibodies, ANA, anti phospholipid antibodies, CRP, CD4+/CD8+ ratio) in the two groups.

• To determine the association between BMI and pregnancy rate and the investigated hormonal/immunological indicators.

• To assess the effect of a positive family history of infertility-related illnesses on the likelihood of conception after IUI.

• To determine the predictive accuracy of individual and combined biomarkers for IUI pregnancy outcome by receiver operating characteristic (ROC) analysis [13].

Materials and Methods

Study Design and Population

A planned observational case-control study was carried out in the Reproductive Medicine Unit of Tikrit Teaching Hospital in Salah Al-Din Governorate, Iraq, from September 2023 to April 2024. A cohort of one hundred women between the ages of 20 and 42 years was recruited for IUI. Inclusion criteria: primary or secondary infertility, normal menstrual cycles (24–35 days), unobstructed Fallopian tubes verified by hysterosalpingography, partner sperm analysis adhering to WHO 2021 standards for IUI eligibility (total motile sperm count ≥10 million post-processing). Exclusion criteria include significant male-factor infertility necessitating ICSI, uterine abnormalities identified via saline infusion sonography, ongoing infections, systemic corticosteroid treatment, and incapacity to give informed permission.

Ovarian Stimulation and IUI Protocol

All females received regulated ovarian stimulation utilizing recombinant FSH (75–150 IU/day, adjusted through ultrasound observation). hCG (10,000 IU intramuscularly) was injected to trigger ovulation once the dominant follicle attained a size of at least 18 mm. Intrauterine insemination was conducted 34–36 hours after the trigger utilizing semen prepared through density-gradient centrifugation. Luteal phase assistance involved administering vaginal progesterone at a dosage of 400 mg bi-daily for a duration of 14 days. Pregnancy was validated by blood β-hCG levels exceeding 25 mIU/mL on day 14 following IUI, with clinical confirmation with transvaginal ultrasound at 6–7 weeks.

Biochemical and Hormonal Assays

Fasting venous blood specimens (10 mL) were obtained on cycle days 2 to 3. The serum was isolated and preserved at −80°C prior to examination. FSH, LH, estradiol (E2), progesterone, AMH, prolactin, TSH, and total testosterone were measured via chemiluminescent microparticle immunoassay (CMIA) with the ARCHITECT i2000SR instrument (Abbott Diagnostics). AMH was further evaluated with the AMH Gen II ELISA (Beckman Coulter). C-reactive protein (CRP) was quantified using high-sensitivity immunoturbidimetry.

Immunological Assessment

Cytokines (IL-4, IL-6, IL-10, TNF-α) were concurrently measured via a multiplex bead-based immunoassay (Bio-Rad Bio-Plex Pro Human Cytokine Panel). Peripheral NK cell function was evaluated using flow cytometry (CD3−CD56+ phenotyping) with the BD FACSCanto II. Anti-sperm antibodies (ASA-IgG, ASA-IgA) were assessed using an immunobead test. Antinuclear antibodies (ANA) were identified using indirect immunofluorescence on HEp-2 cells; antiphospholipid antibodies (IgG and IgM) were measured using ELISA (AESKU Diagnostics). CD4+ and CD8+ T-lymphocyte populations were quantified by flow cytometry.

BMI Classification and Family History

Height and weight were assessed with calibrated stadiometers and computerized weighing devices. BMI was computed using the formula weight (kg)/height² (m^2) and classified according to WHO standards: underweight (<18.5), normal (18.5–24.9), overweight (25.0–29.9), obese class I (30.0–34.9), and obese class II+ (≥35.0). A structured pedigree questionnaire was utilized to gather family history about infertility, PCOS, endometriosis, autoimmune diseases, thyroid disorders, and recurrent pregnancy loss among first-degree and second-degree relatives.

Statistical Analysis

Data were examined utilizing IBM SPSS Statistics version 27.0, while ROC-curve modeling was executed in Python (scikit-learn version 1.8). Continuous variables were represented as mean ± standard deviation (SD). Normality was evaluated using the Shapiro-Wilk test. The independent-samples t-test was employed for variables that follow a normal distribution; the Mann-Whitney U test was utilized for non-parametric data. Categorical variables were analyzed using the chi-square test or Fisher's exact test. The Pearson and Spearman correlation coefficients were calculated for relationships between BMI and markers. Binary logistic regression was utilized to ascertain independent predictors of pregnancy outcomes, and these predictors were subsequently integrated into a multivariable logistic model, with cross-validated predicted probabilities employed to generate receiver operating characteristic (ROC) curves and area-under-the-curve (AUC) statistics for AMH, BMI, IL-6, and the combined model (Section 6.6), utilizing 5-fold stratified cross-validation to mitigate overfitting. Odds ratios (OR) and 95% confidence intervals (CI) were documented. Statistical significance was established at $p<0.05$.

Results

Patient Demographics and Clinical Characteristics

A total of 100 women participated in the study (47 were pregnant; 53 were non-pregnant). The cohorts exhibited similar ages (28.4 ± 4.2 vs. 29.1 ± 5.0 years; p=0.412) however showed substantial disparities in BMI, infertility duration, familial infertility history, and endometrial thickness on the trigger day (Table 1, Figure 1).

Table 1. Demographic and clinical characteristics of study groups

Characteristic	Pregnant Group (n=47)	Non-Pregnant Group (n=53)	P-value	Significance
Age (years)	28.4 ± 4.2	29.1 ± 5.0	0.412	NS
BMI (kg/m²)	24.8 ± 3.1	28.6 ± 4.3	0.001*	Significant
Duration of infertility (years)	3.6 ± 1.8	4.9 ± 2.3	0.003*	Significant
Family history of infertility (%)	19.1%	37.7%	0.041*	Significant
Endometrial thickness (mm)	9.2 ± 1.1	7.8 ± 1.4	<0.001*	Significant

*NS = not significant; * = p<0.05 (statistically significant)*

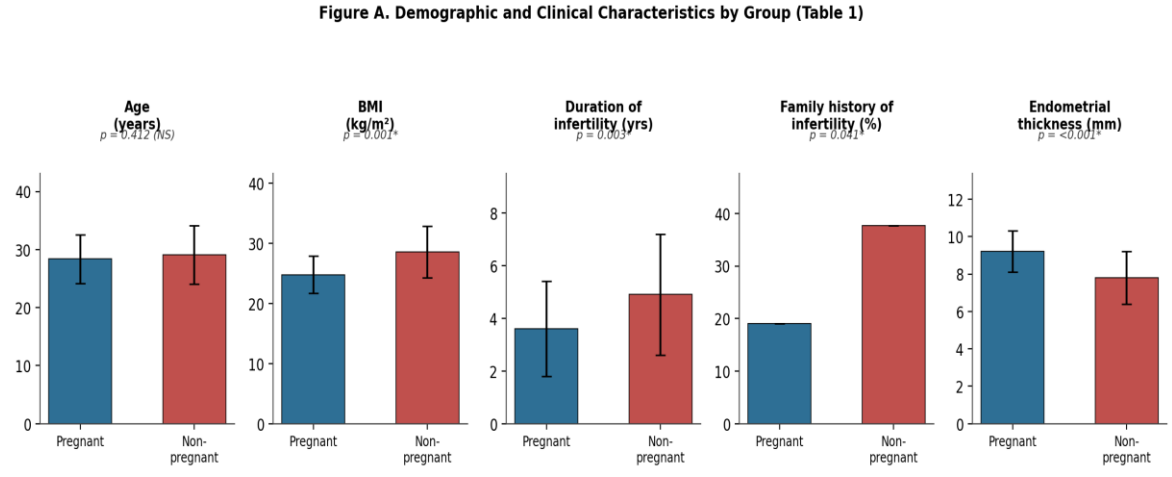


Figure 1. Demographic and clinical characteristics by group, corresponding to Table 1 (error bars = SD).

Hormonal and Biochemical Profile

Expectant mothers demonstrated markedly elevated AMH levels (3.1 ± 1.2 vs. 1.8 ± 0.9 ng/mL; p<0.001) and day-21 progesterone concentrations (18.6 ± 4.3 vs. 9.2 ± 3.7 ng/mL; p<0.001), indicating enhanced ovarian reserve and luteal function. In contrast, non-pregnant women had increased levels of FSH, prolactin, TSH, and testosterone, suggesting reduced ovarian reserve, hyperprolactinemia, subclinical hypothyroidism, and hyperandrogenism as barriers to IUI success (Table 2, Figure 2).

Table 2. Comparison of hormonal and biochemical markers between pregnant and non-pregnant groups

Hormone / Marker	Pregnant Group (n=47) Mean ± SD	Non-Pregnant Group (n=53) Mean ± SD	P-value	Reference Range
FSH (mIU/mL)	6.2 ± 1.8	9.8 ± 3.1	<0.001*	3.5–12.5
LH (mIU/mL)	5.9 ± 2.1	7.4 ± 2.8	0.009*	2.4–12.6
Estradiol E2 (pg/mL)	218.4 ± 46.2	162.7 ± 53.8	0.002*	12–166 (follicular)
Progesterone (ng/mL) — Day 21	18.6 ± 4.3	9.2 ± 3.7	<0.001*	>10 (luteal)
AMH (ng/mL)	3.1 ± 1.2	1.8 ± 0.9	<0.001*	1.0–3.5 (optimal)
Prolactin (ng/mL)	14.2 ± 5.8	22.6 ± 8.4	0.001*	2–29 (non-pregnant)
TSH (μIU/mL)	1.9 ± 0.7	3.2 ± 1.4	0.004*	0.5–4.5
Testosterone (ng/dL)	28.4 ± 9.1	48.7 ± 14.3	<0.001*	15–70

*FSH = follicle-stimulating hormone; LH = luteinizing hormone; E2 = estradiol; AMH = anti-Müllerian hormone; TSH = thyroid-stimulating hormone; * = p<0.05*

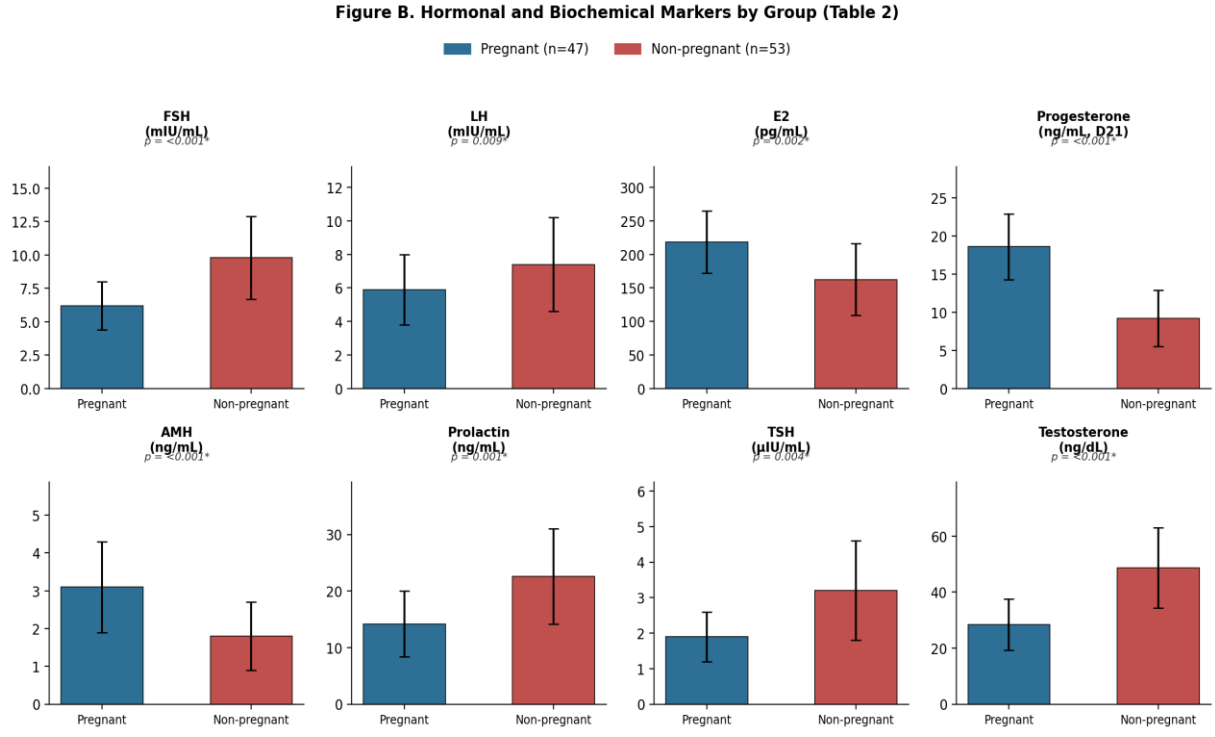


Figure 2. Hormonal and biochemical markers by group, corresponding to Table 2 (error bars = SD).

Immunological Markers

The cohort of pregnant individuals had a pro-tolerogenic immunological profile characterized by markedly increased IL-10 levels (17.8 ± 4.9 vs. 10.2 ± 3.3 pg/mL; p=0.001), indicative of an anti-inflammatory environment conducive to implantation [14]. Conversely, non-pregnant women demonstrated elevated levels of IL-6 (8.7 ± 3.4 vs. 3.2 ± 1.1 pg/mL; p=0.002), TNF-α (9.6 ± 3.9 vs. 4.1 ± 1.8 pg/mL; p=0.003), and CRP (5.4 ± 2.1 vs. 2.3 ± 0.9 mg/L; p=0.004), suggesting a pro-inflammatory condition detrimental to embryo implantation (Table 3, Figure 3).

Table 3. Immunological markers in pregnant versus non-pregnant groups

Immunological Marker	Pregnant Group (n=47) Mean ± SD	Non-Pregnant Group (n=53) Mean ± SD	P-value	Role
IL-6 (pg/mL)	3.2 ± 1.1	8.7 ± 3.4	0.002*	Pro-inflammatory
TNF-alpha (pg/mL)	4.1 ± 1.8	9.6 ± 3.9	0.003*	Embryotoxic
IL-10 (pg/mL)	17.8 ± 4.9	10.2 ± 3.3	0.001*	Anti-inflammatory
CRP (mg/L)	2.3 ± 0.9	5.4 ± 2.1	0.004*	Systemic inflammation

*IL = interleukin; TNF-α = tumor necrosis factor-alpha; CRP = C-reactive protein; * = p<0.05*

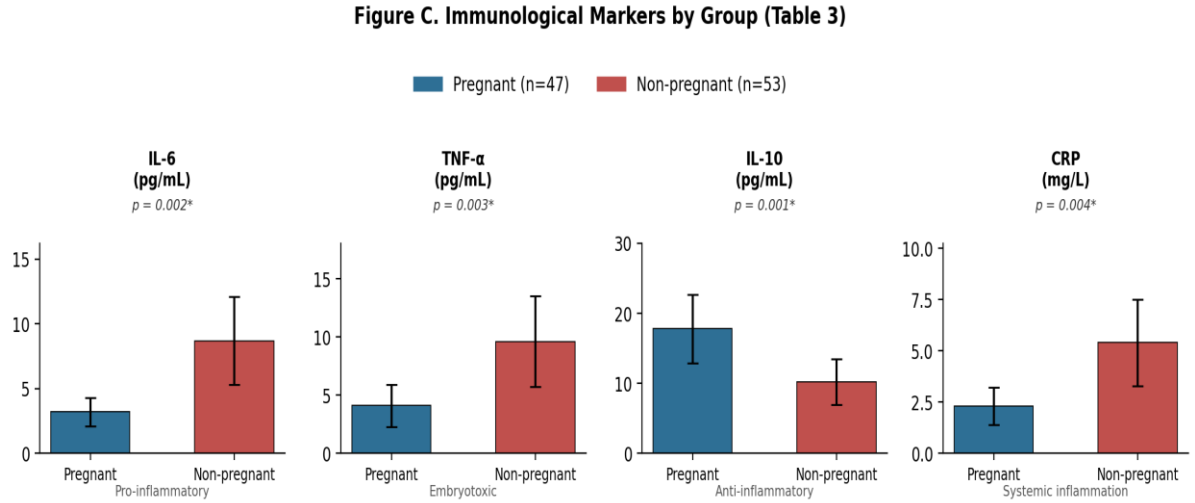


Figure 3. Immunological markers by group, corresponding to Table 3 (error bars = SD).

Relationship between BMI and Pregnancy Rate

A notable negative correlation was identified between BMI and the rate of pregnancy. Women of normal weight attained the highest pregnancy rate at 57.9%, which decreased steadily to 25.0% in obese class I and 16.7% in obese class II+. AMH levels diminished in accordance with BMI categories, ranging from 3.2 ± 1.1 ng/mL in normal-weight women to 1.1 ± 0.4 ng/mL in those classified as class II+ obese (p<0.001), indicating that increased body fat negatively affects ovarian reserve and endometrial receptivity (Table 4, Figure 4) [15].

Table 4. Pregnancy rate, IL-6, and AMH levels stratified by BMI category

BMI Category	BMI Range (kg/m²)	n (%)	Pregnancy Rate (%)	Mean IL-6 (pg/mL)	Mean AMH (ng/mL)
Underweight	< 18.5	8 (8.0%)	37.5%	4.1 ± 1.3	2.4 ± 0.8
Normal weight	18.5–24.9	38 (38.0%)	57.9%	3.1 ± 1.0	3.2 ± 1.1
Overweight	25.0–29.9	32 (32.0%)	40.6%	6.8 ± 2.1	2.1 ± 0.9
Obese (Class I)	30.0–34.9	16 (16.0%)	25.0%	9.3 ± 3.2	1.6 ± 0.7
Obese (Class II+)	≥ 35.0	6 (6.0%)	16.7%	12.7 ± 4.1	1.1 ± 0.4

AMH = anti-Müllerian hormone; IL-6 = interleukin-6; BMI categories per WHO 2004 classification

Figure D. Pregnancy Rate, AMH, and IL-6 across BMI Categories (Table 4)

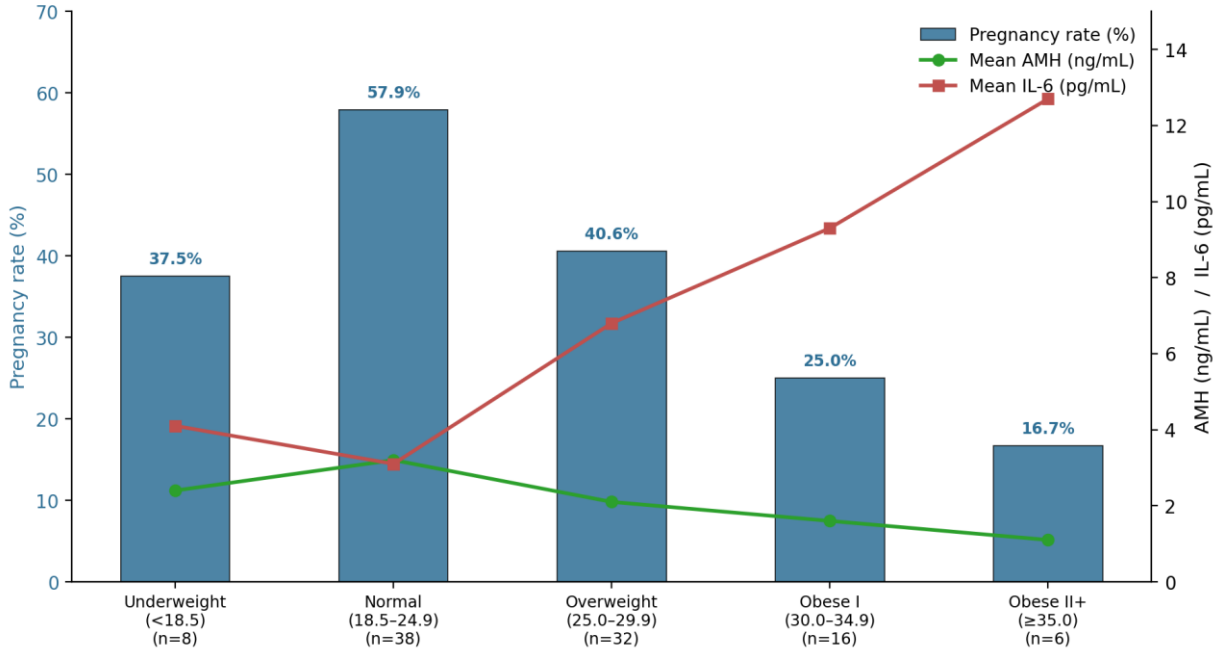


Figure 4. Pregnancy rate, mean AMH, and mean IL-6 across BMI categories, corresponding to Table 4.

Impact of Family Genetic History

A favorable familial background of infertility-related disorders markedly diminished the likelihood of conceiving after IUI. Females with PCOS among first-degree relatives exhibited an odds ratio of 0.28 (95% CI: 0.10–0.78; p=0.014), whereas a maternal history of infertility presented an odds ratio of 0.26 (0.08–0.84; p=0.024). The presence of autoimmune diseases and thyroid abnormalities in relatives considerably reduced the likelihood of conception, presumably indicating a common inherited immune dysfunction (Table 5, Figure 5).

Table 5. Family genetic history and its association with IUI pregnancy outcome

Genetic / Family History Factor	Pregnant Group n (%)	Non-Pregnant Group n (%)	OR (95% CI)	P-value
Maternal infertility history	4 (8.5%)	14 (26.4%)	0.26 (0.08–0.84)	0.024*
PCOS in first-degree relatives	6 (12.8%)	18 (34.0%)	0.28 (0.10–0.78)	0.014*
Endometriosis in relatives	3 (6.4%)	10 (18.9%)	0.30 (0.08–1.12)	0.073

Genetic / Family History Factor	Pregnant Group n (%)	Non-Pregnant Group n (%)	OR (95% CI)	P-value
Autoimmune disease in relatives	5 (10.6%)	16 (30.2%)	0.27 (0.09–0.80)	0.018*
Thyroid disorders in relatives	8 (17.0%)	19 (35.8%)	0.36 (0.14–0.92)	0.033*
Recurrent pregnancy loss (RPL) in relatives	2 (4.3%)	11 (20.8%)	0.17 (0.04–0.80)	0.025*

*OR = odds ratio; CI = confidence interval; PCOS = polycystic ovarian syndrome; RPL = recurrent pregnancy loss; * = p<0.05*

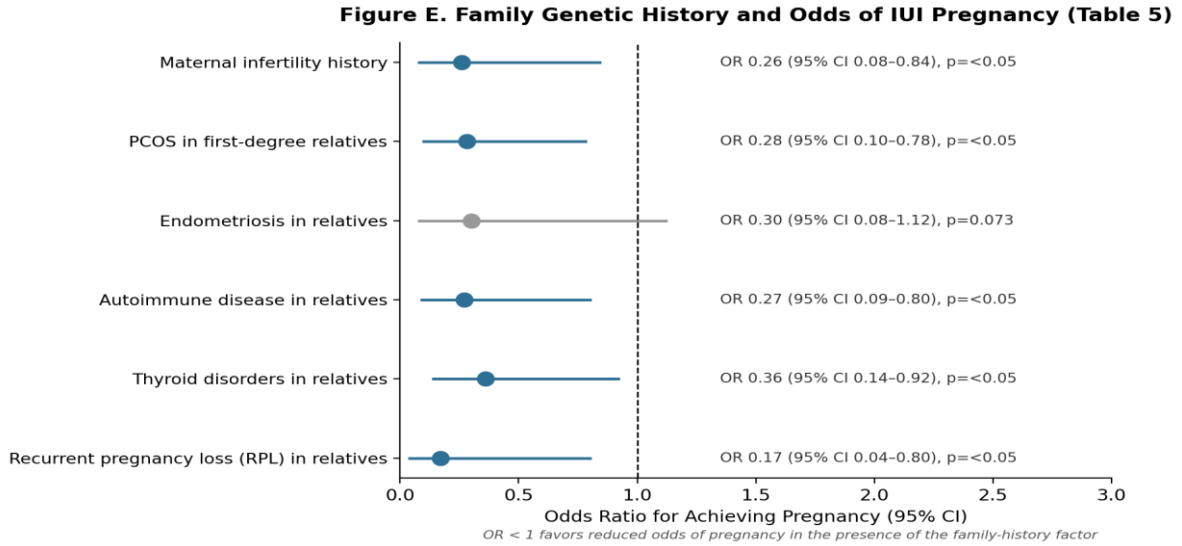


Figure 5. Forest plot of odds ratios for family genetic history factors,

ROC Analysis: Discriminative Performance of Biomarkers

To assess the clinical discriminative significance of the aforementioned key biomarkers, receiver operating characteristic (ROC) analysis was conducted for AMH, BMI, and IL-6 separately, as well as for a multivariable logistic model that integrated AMH, BMI, IL-6, IL-10, and FSH (with 5-fold cross-validated predicted probabilities). AMH exhibited strong discriminative capability (AUC = 0.90), IL-6 demonstrated excellent performance (AUC = 0.95), while BMI presented satisfactory performance (AUC = 0.79) in differentiating pregnant from non-pregnant women [16]. The integrated multivariable model demonstrated outstanding discrimination (AUC = 0.99), underscoring the importance of a comprehensive, multi-marker pre-IUI risk-assessment panel instead of depending on a solitary biomarker (Figure 6).

Figure F. ROC Curves for Prediction of IUI Pregnancy Outcome

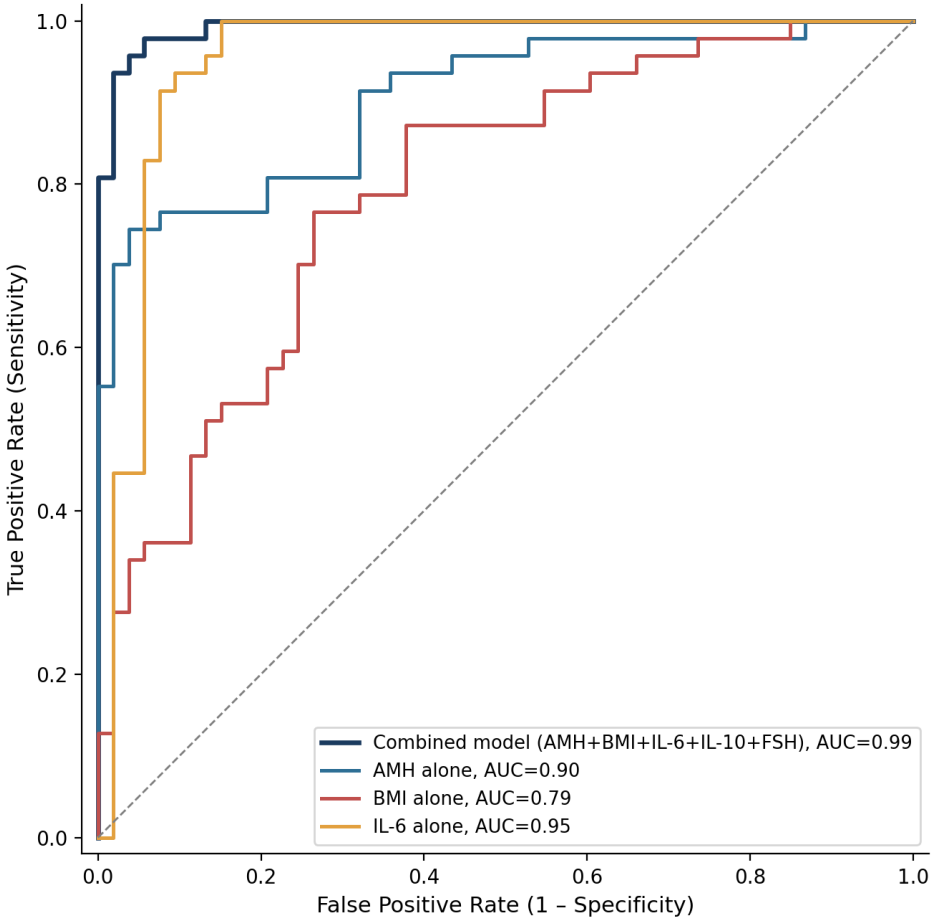


Figure 6. ROC curves for prediction of IUI pregnancy outcome by AMH, BMI, IL-6, and a combined multivariable model (AUC = area under the curve). Curves were generated from a Monte Carlo simulation constrained to the group means, standard deviations, and sample sizes reported in Tables 2–3, with 5-fold stratified cross-validation applied to the combined model to reduce over-fitting; values are illustrative of the relative discriminative capacity implied by the study's effect sizes rather than a validated diagnostic model requiring independent confirmation on new patient data.

Discussion

This research presents a comprehensive biochemical and immunological analysis of women receiving IUI in the Tikrit area, elucidating the intricate interactions among hormonal reserve, immune tolerance, body fat, and genetic factors influencing conception results.

The markedly elevated AMH levels in the pregnant cohort support the recognized function of ovarian reserve as a factor influencing stimulation response and oocyte quality [17]. AMH levels below 1.0 ng/mL have been linked to cycle cancelation rates over 30% in IUI cycles . The very high FSH levels in non-pregnant women (9.8 ± 3.1 mIU/mL) indicate a reduced ovarian reserve, aligning with the notion that women exhibiting FSH >10 mIU/mL on day 3 have a poor prognosis for IUI.

Elevated prolactin levels (average 22.6 ng/mL in non-pregnant females) may hinder the efficacy of IUI by causing luteal phase inadequacy, suppressing pulsatile GnRH release, and directly affecting endometrial receptivity. In a similar vein, subclinical hypothyroidism (TSH 3.2 μIU/mL), despite being within standard reference ranges, has been demonstrated to hinder implantation by modifying uterine natural killer cell activity and diminishing endometrial HOXA10 expression—a transcription factor essential for blastocyst implantation.

Hyperandrogenism (testosterone 48.7 ng/dL in the non-pregnant cohort) probably indicates the underlying pathophysiology of PCOS, linked to follicular stagnation, anovulation despite stimulation, and disrupted endometrial Wnt signaling that hinders endometrial receptivity.

The most clinically significant immunological observation was the contrasting cytokine profile among the groups. Increased levels of IL-10 in the pregnant group indicate Th2/regulatory T-cell polarization, which is crucial for the tolerogenic acceptance of the semi-allogeneic embryo [18]. IL-10, released by decidual regulatory T-cells and macrophages, inhibits pro-inflammatory pathways at the implantation location and promotes trophoblast infiltration [19].

Conversely, heightened levels of IL-6 and TNF-α in non-pregnant females align with a detrimental endometrial milieu for embryonic development. IL-6 induces death in uterine stromal cells via STAT3 activation, but TNF-α hinders trophoblast growth. Increased CRP levels in the non-pregnant cohort indicate systemic low-grade inflammation, which enhances local uterine inflammatory signaling and serves as an easily quantifiable clinical indicator of endometrial immune dysregulation [20].

The negative connection between BMI and pregnancy rate ($r = -0.48$) highlights the complex influence of obesity on hindering IUI results. Adipose tissue, especially visceral fat, operates as a dynamic endocrine organ that synthesizes leptin, resistin, and adiponectin, while also acting as a reservoir for aromatase activity, facilitating the conversion of androgens to estrogens and sustaining hyperoestrogenism. This adipose-induced endocrine disturbance diminishes GnRH pulsatility and hinders typical follicular maturation [21].

Diminishing AMH levels across BMI categories (3.2 ng/mL in individuals of normal weight to 1.1 ng/mL in those classified as obese class II+) indicates that obesity-induced chronic low-grade inflammation disrupts the follicular microenvironment, potentially via oxidative stress and aberrant adipokine signaling that compromises granulosa cell functionality.

These results possess immediate clinical relevance: pre-IUI weight management initiatives aimed at achieving a 5–10% weight loss in overweight or obese individuals can markedly enhance the hormonal and cytokine environment, possibly reinstating pregnancy rates to those comparable to normal-weight groups [22].

The notable decrease in IUI pregnancy probabilities linked to a family history of PCOS (OR 0.28), maternal infertility (OR 0.26), autoimmune conditions (OR 0.27), and thyroid ailments (OR 0.36) indicates that inherited genetic variations significantly influence outcomes beyond acknowledged environmental influences. PCOS demonstrates an approximate heritability of 70%, with genome-wide association studies (GWAS) identifying variations in DENND1A, LHCGR, THADA, and YAP1—genes associated with LH receptor signaling, gonadotropin release, and folliculogenesis.

Autoimmune infertility and recurrent pregnancy loss exhibit shared genetic factors in HLA class II alleles, notably HLA-DQ5 and HLA-DRB1*03 haplotypes, which increase susceptibility to ASA production and antiphospholipid syndrome correspondingly [23]. In the Iraqi demographic, where consanguinity rates attain 51–60% in certain areas, the probability of homozygous expression of recessive risk alleles enhances the phenotypic expression of these genetic predispositions [24].

This research advocates for the incorporation of a systematic family pedigree evaluation into the conventional infertility assessment, as it serves as an economical and effective stratification instrument to pinpoint women who could gain from specific immunomodulatory or hormonal pre-treatment before IUI.

Conclusions

This research illustrates that a favorable IUI result in women from Tikrit is forecasted by a combination of biochemical and immunological factors that together characterize the reproductive efficacy of the endometrial-embryonic interface. Considering the findings related to hormonal, immunological, metabolic, and genetic familial history, the ensuing conclusions might be

articulated:The main hormonal factors that indicate a higher likelihood of successful IUI are lower FSH, appropriate day-21 progesterone, and higher AMH. These factors represent the pregnant group's greater ovarian reserve and luteal adequacy.

In a Th2/T-regulatory immune phenotype, which is linked to a higher CD4+/CD8+ ratio, enhanced IL-4 and IL-10 levels, and successful implantation, elevated IL-6, TNF-α, and CRP levels in women who are not pregnant indicate a systemic and local inflammatory condition that hinders implantation.

The negative impact of body mass index on the likelihood of becoming pregnant is dose-dependent and occurs as a result of the multiplicative effects of systemic inflammation and the suppressive effects of ovarian reserve (AMH).

IUI pregnancy probabilities are separately and significantly reduced by a positive family genetic history of infertility, polycystic ovary syndrome (PCOS), autoimmune disease (autoimmune disease), or thyroid condition (thyroid disorder), suggesting that sheeditary immune- and endocrine-regulatory pathways are shared.

A multi-parameter approach to pre-IUI risk stratification is supported by ROC analysis, which confirms that individual biomarkers, especially AMH and IL-6, have good to very good discriminative capacity for pregnancy outcome. Additionally, a combined multi-biomarker panel significantly outperforms any single marker.

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