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Original Research Article

The Relationship between Waist-to-Hip Ratio, Selected Immunological Markers, Follicular Parameters, and Endometrial Thickness with Intrauterine Insemination (IUI) Outcomes among Infertile Women in Kirkuk, Iraq

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Abstract: ***Background*:** Intrauterine insemination (IUI), whether administered with or without ovarian stimulation, is regarded as a first-line intervention among assisted reproductive technologies for the treatment of infertility. The growing success rates associated with this technique have led many infertile couples to consider it as a preferred initial therapeutic option. ***Aim of Sutdy*:** This study aimed to generate local data to evaluate the relationship between immunological markers—such as Tumor Necrosis Factor (TNF) and antiphospholipid antibodies (aPL)—as well as follicular parameters, endometrial thickness, and waist-to-hip ratio, with intrauterine insemination (IUI) outcomes. The ultimate goal was to improve infertility treatment strategies within the Iraqi community, particularly given the limited local research available in Kirkuk. ***Methods*:** The study involved 96 infertile women who underwent intrauterine insemination (IUI) from December 2023 to February 2025. The association between the variables and pregnancy rates was analyzed using appropriate statistical methods. ***Results*:** Significant differences in follicle size were observed between IUI responders and non-responders across all age groups except the oldest. Endometrial thickness on insemination day differed significantly only in the two older groups. Other variables—number of oocytes, TNF, aPL, and waist-to-hip ratio (WHR)—showed no significant differences across all ages. ***Conclusion*:** The pregnancy rate decreases with the reduction of both endometrial thickness and follicle size, which may reduce the effectiveness of IUI in women experiencing these conditions. ***Conclusion*:** IUI outcomes are influenced by immunological and physiological characteristics, necessitating the management of related conditions before proceeding with IUI treatment.

Keywords: Immunological Markers, Follicular Parameters, Endometrial Thickness.

INTRODUCTION

The failure to attain a clinical pregnancy following one year of consistent, unprotected sexual intercourse is termed as infertility. It is a worldwide health problem that about 48 million couples experience it all over the world as set out by the World Health Organization [1]. Infertility population in couples of IRR age ranges between 10-15 per cent globally [2]. Infertile patients who do not produce children due to thin endometrium, unexplained infertility, mild male factor infertility, or hormonal disorders are normally subjected to assisted reproductive technique (ART) 1st line treatment, which is usually intrauterine insemination (IUI) [3]. Success of IUI does revolve around the kind of ovarian stimulation, the time of insemination, size of follicles, endometrial thickness, sex hormone levels and the count of motile spermatozoa insemination [4]. The reason why IUI is often selected as the first infertility treatment is the ease of use, cost-effectiveness and the less invasive effects of IUI over the other art procedures

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[5]. It can also be said to be fairly safe, and its complications are very few [6]. Success of IUI is dependent on several factors; the stimulation regime, proper timing of the insemination with adequate number of motile sperms, and additional factors like historical number of insemination rounds [7]. Quite a number of specialists advise that IUI should not be used beyond three to four treatment cycles; in case of failure of pregnancy, alternative in other kinds of the ART- in vitro fertilization (IVF) must be applied. This suggestion is informed by facts that after the first four cycles, most pregnancies will have been achieved and little advantage will be gained by further cycles [8]. The stimulation of ovaries is carried out to get a larger amount of oocytes to fertilize with [9]. The elements that decide the rates of pregnancy after IUI include the amount of mature follicles [10]. Follicle size can be used as an indicator of the level of oocyte maturity and is one of the most important factors to obtain high success rates after IUI [11]. Nevertheless, there is still no clear scientific opinion on the size of the optimum follicle needed to achieve successful results [12]. It is recommended that clinicians manage the development of the endometrium and growth of follicles within the infertile couples in their treatment with IUI [13]. Also, there are some immunological agents in the uterus cavity and on endometrium that contribute to a specific pattern of uterine receptivity. Mal-development of vascularity preceding implantation has been linked with abnormal receptivity which reflects absence of standard treatment regimes in matters of suppressing implantation failure particularly with unexplained infertility [14]. Tumor Necrosis Factor (TNF) is one of the mediators of inflammatory system. It has a number of biological effects that can compromise reproductive function since practically all cell types express TNF receptors: activation of immune cascades, immune activation of neutrophils, and induction of collagenase or prostaglandin production. These activities are likely to interfere with the motility of immune cells and hence fertilization potentials [15]. The cells secreting TNF have been shown to be associated with endometrial proliferation and shedding and several conditions including endometriosis, a significant cause of female infertility were shown to be implicated by TNF. High TNF levels were also found in the female reproductive system of women with endometriosis; its direct relation to reproductive disorders is yet to be determined [16]. Antiphospholipid syndrome (APS) is a type of autoimmune disease that is manifested by the prolonged occurrence of blood clots as well as frequent abortions. It is a pathological condition which is related to the arterial and venous thrombosis in uncommon places, including endothelial cell membranes [17]. Waist-to-hip ratio (WHR) is a health measure that can be significant to general obesity and can influence outcome of IUI, particularly in women whose Waist-to-hip ratio is above the normal measures (WHR greater than 0.85) [18]. This research will help to research how being exposed to certain immunological factors, and these are TNF and antiphospholipid antibodies (aPL), may correlate with some physiological aspects, specifically follicular indices, and endometrial thickness, with the outcome of IUI. There is an understanding of how these factors may affect management of their patients who are infertile due to these factors, especially in consideration of the application of IUI. In line with this we carried out a study of the correlations existing between the chosen immunological and physiological variables and clinical outcomes of IUI among various age groups at Al-Ajyal Center of December 2023 to February 2025.

PATIENTS AND METHODS

The sample used in the study consisted of 96 infertile women who applied to the Al-Ajyal Specialized Center in Kirkuk in the period between December 2021 and the final days of February 2025 in order to become pregnant. The women were stratified into two arms depending on the results of intrauterine insemination (IUI) where 18 women showed positive results with a confirmed pregnancy, and 78 women showed negative results with no pregnancies recorded.

Inclusion Criteria

In the husbands, semen analysis report should be normal as per the World Health Organization (WHO) standards. The response up to 30 years for the wives ranged as follows: normal ovaries which did not have cysts in them and especially those in its advanced stages, the fallopian tubes were also normal and the uterus was normal in shape without any deformity. Hysterosalpingography (HSG) ascertained the uterine and tubal conditions.

Procedure

The procedure of intrauterine insemination (IUI) cycle included the selection of eligible couples and elimination of couples who are not responsive to the parameters of the study by carrying out relevant tests based on inclusion criteria.

Procedures of Husband Selection

A semen analysis of husbands was done when they had not had any intercourse within three to five days. Husbands with semen parameters that matched with those standards mentioned by the World Health Organization (WHO) were chosen whereas those who failed to match with the standard were excluded.

Procedures of Wives Selection

In the research, the wives between 20-40 years were selected. The second day of menstrual cycle was used to obtain the initial estimate of endometrial thickness, the fallopian tube status, uterine shape and ovaries by performing pre-contrast radiographic imaging of uterus done using contrast dye. The wifes that met the study criterion were selected and those that fell out of the criterion were left out. The waist to hip ratio was also measured.

Intrauterine Inseminating (IUI) Procedures

Couples who could meet the criteria set in the study were chosen. On the second day of the menstrual cycle, Ovarian stimulation was started by letting agents which are Letrozole capsules, 2.5 mg, of Swiss origin, and used as follows: a five-day administration, starting at the second day of the menstrual cycle. Ultra sonogram examination was also set at a schedule to check on the growth of mature follicles and the thickness of the endometrial lining. Besides, tumor necrosis factor (TNF) and antiphospholipid antibodies levels were determined.

Ultrasound follow-up began on the day 9 of menstrual cycle, day 11 and day 13 to measure the follicular growth. Depending on the maturation of follicles, the 1000 international units dose of human chorionic gonadotropin (HCG) (Pharma Levzon, China) was administered by an injection. It was recommended that the husband avoid sexual intercourse 3 to 5 days preceding the procedure of intrauterine insemination.

At the time between 24 to 36 hours of injecting HCG, semen specimen of the husband was collected, washed, and separated under the Density-Gradient sperm separation technique as dictated by the manufacturer and guidelines.

Intrauterine Insemination-(IUI)-Procedure

The semen of the husband was prepared using the Density-Gradient sperm separation method after being sent in the manufacturer-prescribed instructions and guidelines and 0.8 ml of the prepared sperms was obtained through a sterile insemination catheter. The catheter was attached to syringe and semen was gently injected in the uterus through the cervix. The filling of the bladder is necessary during the process. Normal saline irrigation was applied to the area before insemination. The wife was maintained at the same position not less than 20 minutes after the procedure. After the insemination process, the wife was requested not to have intercourse within three days.

Stages of Pregnancy Detection

The assessment of the reaction to intrauterine insemination (IUI) as well as the verifying of pregnancy can be done in two steps. Its application involves the initial step which is done 14 to 17 days after the insemination by determining the beta-hCG serum. The second step is aimed to verify the reaction to IUI and is completed with a transvaginal ultrasound with contrast (sonohysterography), which normally followed after IUI procedure five to six weeks later.

Statistical Analysis

The result of this research work meant to establish the level of the hormone HCG in the serum of the wives 14 17 days after the intrauterine insemination (IUI). The HCG concentration of more than 25 IU/mL was regarded as a sign of positive response to the procedure and confirmed achievement of pregnancy, and meeting the purpose of the study. As opposed to that, an HCG level that measures less than 25 IU/mL showed the absence of response to the IUI process and a failure to become pregnant. In case of positive response, it was confirmed within five to six weeks of the IUI procedure by the use of transvaginal ultrasound with the contrast (sonohysterography) observing the presence of the gestational sac. It was carried out with the ANOVA test and it was related to letter-based notation (A/B). Comparison of means was made by ANOVA and statistically significant differences were indicated by the letters A and B-whereas identical letter denoted non-significant difference. Continuous variables were expressed as mean with standard deviation (SD) and their comparisons were performed by T-test. IUI treatment cycles were subjected to groups based on an age range. The result obtained was regarded as significant at P-value <= 0.05. Some of the confounding factors to be considered were age of wives, follicular parameters, tumor necrosis factor (TNF), antiphospholipid antibodies (aPL) and waist-to-hip ratio (WHR).

Intrauterine Insemination (IUI) Outcomes

A statistically significant decrease in the clinical pregnancy rate was observed with the reduction in endometrial thickness in the age groups 30–35 years and 36–40 years. However, no significant difference was observed in the younger age groups.

Regarding follicle size, a significant decrease in the mean follicular diameter was noted among non-responders compared to responders across all age groups, except in the oldest age group (36–40 years), where no significant difference was detected between responders and non-responders to IUI. In the youngest age group (20–25 years), the mean endometrial thickness in responders with a positive pregnancy outcome was (10.00 ± 0.597) mm, while in non-responders with a negative outcome it was (8.984 ± 0.219) mm.

The mean follicular diameter in this group was (21.00 ± 0.267) mm in responders and (18.46 ± 0.454) mm in non-responders. In the age group (26–30 years), the mean endometrial thickness in responders with a positive outcome was (9.500 ± 0.866) mm, compared to (8.900 ± 0.344) mm in non-responders. The mean follicular diameter was (21.00 ± 0.577) mm in responders and (18.50 ± 0.312) mm in non-responders. In the age group (31–35 years), the mean endometrial thickness in responders was (11.00 ± 0.577) mm, whereas in non-responders it was (8.00 ± 0.206) mm.

The mean follicular diameter in responders was (22.00 ± 1.154) mm, compared to (18.30 ± 0.291) mm in non-responders. In the oldest age group (36–40 years), the mean endometrial thickness in responders with a positive pregnancy outcome was (11.00 ± 0.00) mm, compared to (8.10 ± 0.460) mm in non-responders. The mean follicular diameter in responders was (18.46 ±

0.00) mm, while in non-responders it was (18.33 ± 0.512) mm.

Table 1: Shows the Effect of Endometrial Thickness, Follicle Size, and Number of Follicles on the Outcome of IUI across Different Age Groups

Number of eggs Count	Largest egg size (mm)	Endometrial Thickness(mm)	Age groups
2.500±0.327 A	21.00±0.267 A	10.00±0.597 A	20-25 year Positive
2.384±0.167 A	18.46±0.454 B	8.984±0.219 A	20-25 year Negative
2.500±0.288 A	21.00±0.577 A	9.500±0.866 A	26-30 year Positive
2.400±0.210 A	18.50±0.312 B	8.900±0.344 A	26-30 year Negative
2.00±0.577 A	22.00±1.154 A	11.00±0.577 A	31-35 year Positive
1.700±0.146 A	18.30±0.291 B	8.00±0.206 B	31-35 year Negative
2.500±0.00 A	18.46±0.00 A	11.00±0.00 A	36-40 year Positive
2.00±0.288 A	18.33±0.512 A	8.10±0.460 B	36-40 year Negative

As for the number of follicles on the day of intrauterine insemination, the waist-to-hip ratio, and the serum levels of both tumor necrosis factor (TNF) and antiphospholipid antibodies (aPL), no statistically significant differences were found in our study across all age groups.

Table 2: Shows the Effect of WHR, TNF, and APL on the Outcome of IUI across Different Age Groups

Apl (u/ml)	TNF-α (pg/ml)	WHR	Age groups
0.595±0.010 A	4.754±0.296 A	0.775±0.0193 A	20-25 year Positive
0.609±0.024 A	5.150±0.253 A	0.803±0.009 A	20-25 year Negative
0.540±0.005 A	4.010±0.057 A	0.774±0.008 A	26-30 year Positive
0.592±0.029 A	3.582±0.189 A	0.805±0.011 A	26-30 year Negative
0.440±0.063 A	3.920±0.023 A	0.775±0.014 A	31-35 year Positive
0.600±0.025 A	4.187±0.133 A	0.833±0.016 A	31-35 year Negative
0.490±0.00 A	4.910±0.00 A	0.860±0.0 A	36-40 year Positive
0.646±0.034 B	4.570±0.254 A	0.821±0.008 A	36-40 year Negative

DISCUSSION

Intrauterine insemination (IUI) outcomes are affected by a variety of factors and, among them, there are the endometrial thickness and some of the follicular parameters including the follicle size on the day of an insemination [19]. This paper was intended to explore the correlation of endometrial thickness, and follicular parameters (number and sizes) and waist-hip ratio (WHR) and clinical pregnancy outcomes after IUI. Stages of wives in the participating women were classified in to four in between 20 to 40 years: (2025 years), (2630 years), (3135 years), and (3640 years). The findings in the study presented in this paper indicated that positive outcomes of IUI reduced as endometrial thickness diminished in the two older age groups between non-responders and responders. The results are in tandem with those of Weisman *et al*., who published results indicating decreased response rate to IUI with reduced endometrial thickness as well as increased age [20]. Also, there was a large decline of the size of the follicle found at the insemination day on the non-responders when compared to the responders on all the

ages other than the oldest in this research. The result is also consistent with other studies that showed that the smaller the size of the follicle, the smaller the likelihood of IUI success [21]. Whereas, the current study demonstrated no difference was found in the rate of mature follicles on day 3 between non-responders and responders, which is in tandem with the previous reports stating that presence of three or more mature follicles on the day of insemination reduces the chances of success of IUI [22]. In addition, there was a substantial difference between non-responders and the responders in the case of waist-to-hip ratio wherein non-responders had a higher value in terms of waist-to-hip ratio than the responders. This finding is in line with other research results indicating that fat distribution due to obesity among individuals does not have a great influence on the outcomes of IUI [23]. There was no considerable disparity in tumor necrosis factor (TNF) levels among the responders and the non-responders in agreement with Liu *et al*., [24].

CONCLUSION

In reduced endometrial thickness the response rate to intrauterine insemination (IUI) is lesser especially in the age bracket of 30 to 35 years and 36 to 40 years. It also reduces with a smaller follicle size in the day of insemination in all age groups except the tallest one (3640 years) for which actually no distinction was made between patients responding to IUI and those who were not who better responsed. Moreover, differences did not appear large between the responders and non-responders concerning tumor necrosis factor (TNF), antiphospholipid antibodies (aPL) and finally waist-to hip ratio (WHR).

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