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Sonographic Association of Endometrial Thickness at Proliferative Phase in Infertile Females

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Abstract

Objectives: To determine the sonographic association of endometrial thickness at the proliferative phase in infertile females. **Study Design:** This Cross-sectional observational. **Place and duration:** Government Nawaz Sharif Hospital yakki gate Lahore 10st March 2017 to 10th September 2018. **Methodology:** This Cross-sectional observational study was conducted at Government Nawaz Sharif Hospital yakki gate Lahore 10st March 2017 to 10th September 2018. Ultrasound (Mindray (Dc-3)) with the convex transducer, frequency ranging 3-6 Mhz was used. All 103 participants were scanned trans abdominally in the supine position with full urinary bladder. **Result:** By using independent sample test with the help of SPSS 25 that evaluates Levine's Test for Equality of Variances and t-test for Equality of Means. The t-test for Equality of Means shows there was a statistically significant association between endometrial thickness and infertility. **Conclusion:** Thick endometrium is more favorable for implantation as compared to thin endometrium. By comparing the mean of endometrial thickness, it was observed that the mean endometrial thickness in fertile females was greater than infertile females.

Keywords: Infertility, Endometrial Thickness, Endometrial Blood Flow, Ultrasound

INTRODUCTION

Infertility is one of the most common Social, economic, Psychological and medical problems in the female of childbearing age^{1,2}. Infertile women and men have reported experiencing depression, helplessness, and marital strain. Major depression related to infertility is 2–3 times as common in women as in men^{3,4}. The clinical definition for infertility proposed by WHO and International Committee for Monitoring Assisted Reproductive Technologies, as “a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse”⁵. In under-developed countries, the 12-month prevalence rate ranges from 6.9 to 9.3%. Substantial geographic differences in the prevalence are noted, and these differences are largely explained by different environmental, cultural and socioeconomic influences^{6,7}. The overall reported prevalence of infertility was 12.5% among women and 10.1% among men⁸. Although the population of Pakistan is rapidly increasing its population growth rate is around 2%, its rate of infertility is

21.9% (primary and secondary 3.5%, and 18.4% respectively)⁹. There are numerous of infertility but the most common causes include problems with ovulation (Hormone imbalance, Tumor or cyst, use of various medicine, Thyroid gland pathologies, obesity, Stress), Intense exercise that causes a significant loss of body fat, Extremely brief menstrual cycles, damage to fallopian tubes or uterus (Pelvic inflammatory disease, A previous infection, Polyps in the uterus, Endometriosis or fibroids, Scar tissue or adhesions, Chronic medical illness, Previous ectopic (tubal) pregnancy, Birth defect), or problems with the cervix. Age, Abnormal cervical mucus, and deficient endometrial preparation contribute to infertility^{10,11}.

Endometrial preparation for the implantation of the zygote is one of the key features of fertility and is called decidual reaction¹². Decidualization succeeds when pregnancy occurs and subjected to further development¹³. The endometrium is the inner lining of the uterus. it is a mucosal lining and changes in thickness throughout the menstrual cycle¹⁴. Endometrium thickness changes throughout the menstrual cycles¹⁵. The menstrual cycle has three phases; menstrual phase, proliferative phase, and secretory phase¹⁶. The menstrual changes in the endometrium are essentially degenerative. The coiled arteries undergo vasoconstriction a few hours before the onset of menstrual bleeding. The Proliferative phase, define the regeneration of endometrium and lasts until the 14th day of a 28 day of the cycle. Secretory phase is referred to the further hypertrophy of endometrium so that immediately before menstruation its average thickness is about 8 to 10mm^{16,17}. Deficient decidualization can lead to poor implantation and ultimately early loss of pregnancy and infertility¹⁷. Following ovulation, the luteal phase of a natural cycle is characterized by the formation of corpus luteum, which secretes steroid hormones estrogen and mainly progesterone¹⁸. Progesterone is essential for secretory transformation of the endometrium that permits implantation as well as maintenance of early pregnancy¹⁹. Luteal phase insufficiency is one of the reasons for implantation failure, which has been responsible for the failure of many cases of pregnancies and assisted reproduction^{20,21}. The endometrial preparation (decidualization) could be assessed by various imaging methods, but Ultrasound is one of the best and safe method to measure the thickness of endometrium for as determinant of decidualization²². A few of the most common anomalies are discussed²³.

Sonographic appearance of the endometrium is very reliable and accurate imaging method to measure it during entire cycle¹⁵. The reliability of transvaginal as well as trans abdominal sonographic is within clinically acceptable limits²³. With the developments of the machines and introduction of the high-resolution transducer in state of the art modalities, improved the accuracy of ultrasound in the measurement of endometrium²⁴.

The purpose of this study was to assess the association of infertility with endometrial thickness. There are many causes of infertility, but it is postulated that deficient endometrial thickness is one of them. As it is obvious from the discussion in the context of previous studies that endometrial thickness plays a crucial role in the implantation of the zygote and deficient decidualization can lead to infertility. The researcher, therefore, intended to compare the endometrial thickness with infertility so that the alarming situation may be highlighted.

METHODOLOGY

Sampling technique is convenient sampling, and the sample size is 103 including for both genders which are calculated from the prevalence of infertility (7%) with the following sample power formula, $n = z^2(pq)/d^2$. This Cross-sectional analytical study was conducted at Government Nawaz Sharif Hospital yakki gate Lahore 10st March 2017 to 10th September 2018. Ultrasound (Mindray (Dc-3)) with the convex transducer, frequency ranging 3-6 Mhz was used. All 103 participants were scanned trans abdominally in the supine position with full urinary bladder. All the females with primary and secondary infertility at fertile age group and all the fertile females from the same population are included. All infertile females with uterine anomalies and females with an ill-defined, undifferentiated uterus are excluded.

RESULTS

All the 103 patients calculated with sample power equation were scanned, having to mean age 31.42 ± 5.304 (19 to 43). Mean age at the time of marriage of all females was 23.06 ± 2.95 (18 to 33) and the mean endometrial thickness was 6.24 ± 2.11 (3 to 12) mm. Frequency distribution of the participants among fertile females, Primary infertility, and secondary infertility was 57 (55.3%), 32 (31.1%), and 14 (13.6%). All the participants

were divided into a different class with a class width of 5, their frequency and percentage are summarized in Table 1. The thickness of the endometrium was classified in three classes with class width of 3mm, the frequency, and percentage of ≤ 6 mm 61 (59.2%), 7-9 mm 34 (33%), and 10+ mm 8 (7.8%). Independent t-test was used to compare the mean of the endometrial thickness in fertile and infertile females. The mean endometrial thickness in 57 (55.33%) fertile females was 7.28 ± 2.024 mm, while in 46 (44.775) infertile females were 4.96 ± 1.398 mm. Distribution of fertile, primary infertility and secondary infertility in classes of age (years) is shown in Figure 1. Distribution of fertile, primary infertility and secondary infertility in classes of endometrial thickness (mm) is shown in Figure 2. A significant association of endometrial thickness was estimated with fertility, primary infertility and secondary infertility cases, while using Analysis of variance (ANOVA). Calculated p-value was 0.000, which reflect a significant association. Multiple Comparison Test was used to compare the mean of endometrial thickness in 32 (31.06%) Primary infertility, 14 (13.59%) Secondary infertility, and 57 (55.33%) fertile women was 4.88mm, 5.14mm, and 7.28mm respectively. No significant difference between the endometrial thickness of primary and secondary infertility was noted with multiple comparison Test reveals (p-value 0.89) (Figure 3), while endometrial thickness infertile women and primary/secondary infertility was significant with p-value 0.000 each.

Table I: Frequency and percentage of Age groups of the participants.

Groups of Age (year)	Frequency	Percent
≤ 25	16	15.5
26 - 30	30	29.1
31 - 35	31	30.1
36 - 40	25	24.3
41+	1	1
Total	103	100

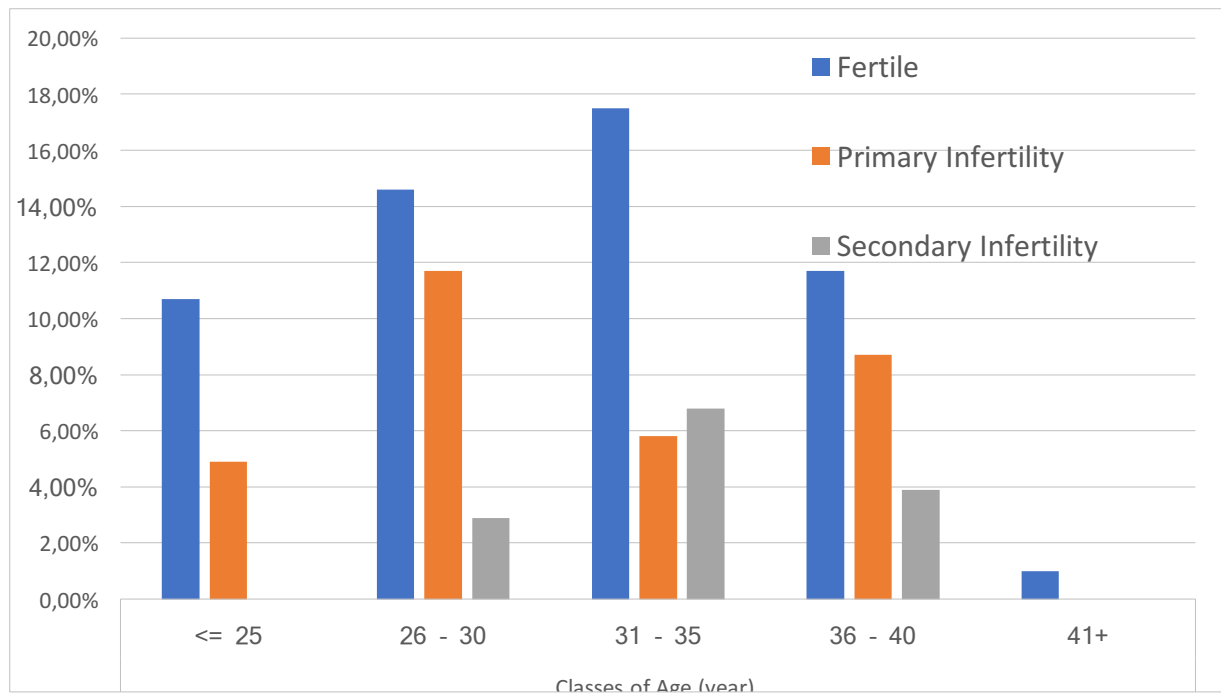


Figure I: Classes of age in years versus fertility/ infertility cross-tabulation

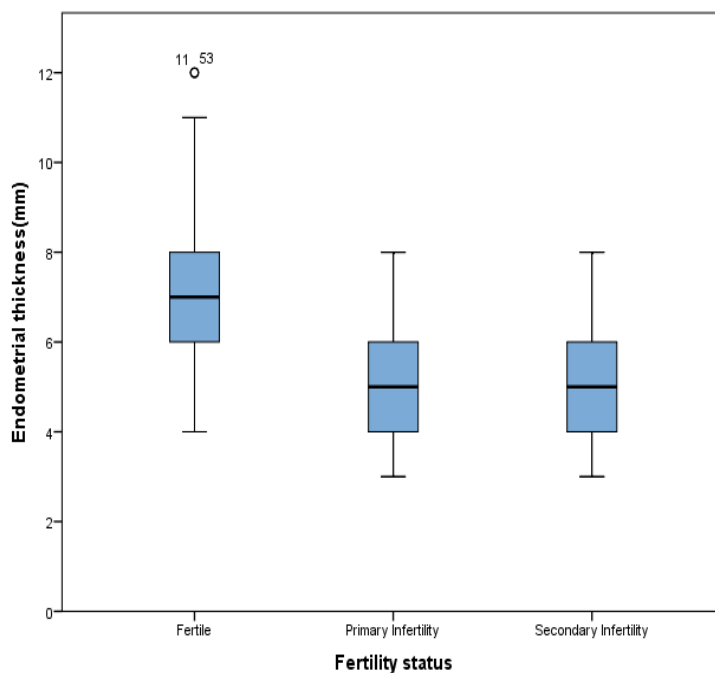


Figure II: comparison of the mean of endometrial thickness in Primary infertility, Secondary infertility, and fertile women.

DISCUSSION

Decasualization is the preparation of endometrium for the implantation fertilized ovum. Capability Endometrial preparation has an effect on receptivity to some or great extent. Very well prepared thick, fully nourished, and vascularized endometrium have more chances to conceive than unprepared, thin, avascular endometrium. Endometrial thickness was greater in cycles resulting in pregnancy than in cycles not resulting in pregnancy. The results of the study show that pregnancy rate was gradually increased from 53% females having an endometrial lining of <math>< 9\text{ mm}</math>, to 77% of females with an endometrial lining of $\geq 16\text{ mm}</math>. ²⁷ It was therefore concluded that the$

rate of favorable pregnancy outcomes increases significantly with an increase in endometrial thickness, independent of the effects of patient age and embryo quality. Increased endometrial thickness predicts the likelihood of normal intrauterine pregnancies²⁸. Shireen J Sathar et al. studied to explore the impact of industrialization, promotion of education, female employment, urbanization, and migration on proportions never married Pakistani population²⁹. By studying data for the various era in time, the mean age for female marriage was calculated in 1961 as 18.1 years, in 1972 as 19.8 years, and in 1981 as 20.7 years. According to this data, the expected mean age for marriage in 2021 will be 24.3 years. Schemes of marriage behavior were expected to vary in Punjab, Sind, NWFP, and Baluchistan, due to cultural variations, different levels of development, and variations in urbanization. Punjab had the highest proportions of never married females both in urban and in rural areas. The much more unmarried individual was calculated in 15-19 years' age group, in Punjab, which is considered the most developed province. Never married proportion in the different provinces was significant especially for females than for males. The mean age at the time of marriage was calculated as 23.06 ± 2.95 years, which was proportionally increased with industrialization. In the current study, the mean age of females at the time of marriage was similar to the estimated age proposed by previous studies.

To investigate the role of sonography in the assessment of endometrial receptivity, 135 individuals were transvaginal studied. Association between implantation rate and spiral artery blood flow and between implantation rate and endometrial thickness was calculated. Mean endometrial thickness was 11.4 ± 2.8 mm (4.9 to 21.1)³⁰. To examine the association between medicated frozen-thawed embryo replacement (FER) outcomes and endometrial thickness, a retrospective observational study was conducted. The endometrial thickness 7 mm and heights than 14mm were associated with the lowest pregnancy rates. In those cycles in which endometrial thickness was 9 to 14 mm, significantly higher implantation rates were achieved as compared to 7 to 8 mm endometrial thickness³¹. In the current study, fertile and infertile female were included; therefore the overall mean endometrial thickness is less than the previous studies. Endometrial thickness was greater for fertile age group but lesser for infertile. In the current study, all the participants were divided into three groups; fertile group, primary and secondary infertility. The mean endometrial thickness was almost similar in primary and secondary infertility, moreover, there was less variation in the endometrial thickness of these groups as how in boxplot (Figure 3).

Boivin et al. conducted a study in 2007, for the estimation of infertility prevalence and proportion of couples seeking treatment⁷. The 12-month prevalence prevalence of infertility was estimated as 9%, in more developed countries 3.5% to 16.7% range, while in less-developed nations the range was 7.0% to 9.3%. In developed countries about 56.1% of couples seeking treatment amongst the total infertile couples. But in underdeveloped countries, about 51.2% of the couples seeking treatment. Based on the current world population survey and these estimates, currently about 72.4 million women are infertile; amongst them, about 40.5 million are currently seeking for infertility treatment. The Prevalence of primary and secondary infertility was estimated in the tertiary center in eastern Saudi Arabia by Haifa A.Al-Turki, through a retrospective study in 2015³². In this study, 2414 patients were randomly selected from the multiple clinics of obstetrics and gynecology department of the hospital. It was estimated that 18.93% of the total female population was infertile. Among these infertile females, 78.99% were primary infertility, and 21.01% were secondary infertility. It was concluded that that the prevalence of primary infertility was more common as compared to secondary infertility. The current study agrees with the international data, and we also observed that the prevalence of primary infertility (74.4%) was more than that of secondary infertility (25.6%) as shown in Table 2, Figure 2.

Kevin S. Richter studied 1294 infertile patients were in 2016, to evaluate the relationship between endometrial thickness and fetal outcomes of "In Vitro Fertilization". The thickness of the endometrium was greater in cycles resulting in pregnancy than in cycles wherein there is no pregnancy. According to the study pregnancy rates gradually increased from 53% in patients with an endometrial thickness of less than 9 mm, to 77% in patients with an endometrial thickness more than 16 mm. Significant effects of age, embryo quality, and endometrial thickness on both pregnancy rates and live-birth were calculated through multiple logistic regression analysis. There was a weak association between decreasing rates of spontaneous abortion with increasing endometrial thickness. It was concluded that the chances of live birth increase significantly with an increase in endometrial thickness²⁷. A significant association between endometrial thickness and fertility was found in the current study.

CONCLUSION

Thick endometrium is more favorable for implantation as compared to thin endometrium. By comparing the mean of endometrial thickness, it was observed that the mean endometrial thickness in fertile females was greater than infertile females.

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