

# **“THE ASSOCIATION OF MEAN FOLLICULAR DIAMETER AT THE TIME OF OVULATION TRIGGER AND CONCEPTION RATE AFTER INTRAUTERINE INSEMINATION”**

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## **INTRODUCTION**

Infertility is defined as “failure to conceive after one year of unprotected intercourse”. Primary infertility means that the couple has never conceived. Secondary infertility means that the couple has experienced a pregnancy before and failed to conceive later<sup>1</sup>. Infertility affects up to 15% of reproductive-aged couples worldwide. According to World Health Organization estimate, the overall prevalence of primary infertility in India is between 3.9 to 16.8%<sup>2</sup>.

Intra- Uterine Insemination (IUI) is the simplest method of assisted reproduction as it is inexpensive and easy to perform with a success rate per cycle ranging between 10% to 30%<sup>3,4</sup>. There are a number of factors which determine the success of Intrauterine insemination such as patient characteristics, type of ovarian stimulation and number of inseminations in each cycle<sup>3</sup>. One such factor which has received little attention is the Mean Follicular Diameter (MFD) before triggering ovulation with human chorionic gonadotropin (hCG).

It is commonly accepted that the size of the ovarian follicles should be neither “too small” (unable to respond appropriately to trigger administration and produce a mature oocyte) nor “too large”, (as the post-mature follicles may not be competent for fertilization)<sup>5,6</sup>. The estimation of appropriate size of the follicle will enable the accurate determination of trigger efficacy and that will yield the information on the precise timings for the trigger<sup>7</sup>.

Various studies have shown the influence of the number of follicles and MFD for the determination of the success of IUI technique<sup>8,9</sup>. This study aims to study the role of MFD and the factors associated in the determination of the success of IUI.

## **RESEARCH QUESTION**

Is there any association of mean follicular diameter at the time of ovulation trigger with conception rate after Intrauterine Insemination?

## **MATERIALS AND METHODS**

### **Inclusion criteria-**

- i. All infertile females between 18-40 years of age planned for controlled ovarian stimulation (with Clomiphene Citrate or Letrozole) followed by IUI
- ii. Women who undergo IUI for the first time
- iii. At least one patent tube
- iv. For males, total motile sperm count (post wash) more than 5 million
- v. Couples who are willing to give informed consent

### **Exclusion criteria-**

- i. Diagnosed pelvic pathology which can affect the outcome like Severe endometriosis, severe adenomyosis, uterine fibroid, endometrial polyp, severe pelvic adhesions, uterine anomaly

### **Brief methodology-**

This was a prospective observational study conducted in department of Obstetrics and Gynaecology, AIIMS, Raipur from October 2019 to March 2021. All women who were planned for IUI after Ovulation Induction (with Clomiphene Citrate or Letrozole) and those who fulfilled the inclusion and exclusion criteria were enrolled for the study. Partner with TMSC >5 million was included. The first cycle that was conducted was selected for the study. All patients were followed up from day 2 of cycle. As per the standard protocol of IUI, Ovulation induction (with Clomiphene Citrate or Letrozole), serial follicular monitoring were done. Later, ovulation trigger was given. The Mean Follicular Diameter (MFD) at the time of ovulation trigger was noted and participants were divided into 4 groups:

Group A: MFD  $\leq$  18 mm

Group B: MFD 18- 20 mm

Group C: MFD 20-22 mm

Group D: MFD >22 mm

IUI was performed after 36 hours of hCG injection. Luteal phase support for next 14 days were given from the day of IUI. Urine Pregnancy Test (UPT) was advised after missed periods and result were noted.

### TABLES AND OBSERVATIONS

**Table 1- Comparison of basic variables in study groups**

Basic Variables		MFD ≤18 mm	MFD 18.1-20 mm	MFD 20.1-22 mm	MFD >22 mm	P value
Age (years)	Mean ± SD	30.44±4.30	29.91±4.43	27.75±3.00	27.55±2.18	0.098
BMI (Kg/m <sup>2</sup> )	Mean ± SD	23.5±1.63	23.47±3.06	23.17±2.48	23.20±3.55	0.978
Duration of infertility (years)	Mean ± SD	5.33±2.78	4.78±2.74	3.92±3.15	3.33±1.41	0.310

Table 1 shows basic variables like age, BMI and duration of infertility in study groups. One-way ANOVA test was used for evaluation of basic variables in study groups. The above table shows that there were no significant difference between mean age, BMI and duration of infertility in the study groups.

**Table 2- Mean Follicular Diameter and IUI outcome**

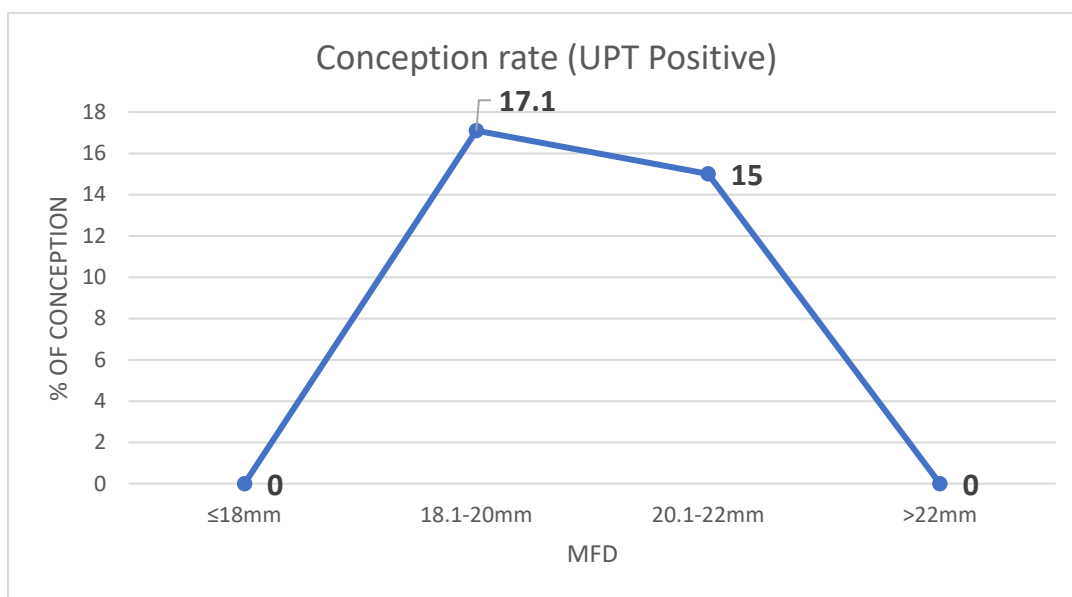
UPT positive	N	Average of MFD	Standard Deviation of MFD	Standard Error Mean	p-value
Yes	9	19.433	1.164	0.388	0.357
No	64	19.974	1.689	0.211	

Table 2 shows comparison of MFD and IUI outcome. Among the women who conceived (UPT positive), the smallest follicular size at the time of ovulation trigger (hCG injection) was 18.269 mm and the largest follicular size was 20.597 and the average of MFD in those who conceived was 19.433. Among those who did not conceive (UPT negative), the smallest follicular size was 18.285 and the largest follicular size was 21.663 and the average of MFD in those who did not conceive was 19.974. No statistically significant difference in MFD was found between women who conceived and who did not conceive.

**Table 3- Conception rate (UPT positive) in study groups**

UPT positive	MFD ≤18 mm N (%)	MFD 18.1-20 mm N (%)	MFD 20.1-22 mm N (%)	MFD >22 mm N (%)	Total	P value
Yes	0 (0)	6 (17.1)	3 (15)	0 (0)	9 (12.3)	0.332
No	9 (100)	29 (82.9)	17 (85)	9 (100)	64 (87.7)	
Total	9 (100)	35 (100)	20 (100)	9 (100)	73 (100)	

Chi-square test;  $p > 0.05$  not significant



**Figure 1- Graph of conception rate in study groups**

Table 3 shows that out of the 73 undergone IUI, 9 (12.3%) become pregnant successfully (turned out to be UPT positive). The study subjects were grouped into Group A: MFD ≤18 mm, Group B: MFD 18.1- 20 mm, Group C: MFD 20.1-22 mm, Group D: MFD >22 mm. The outcome of IUI were observed among the groups and the 18-20 mm and 20-22 mm group achieved successful pregnancy in 17.1% and 15% of the study subjects respectively, whereas all the patients with MFD ≤18 mm and >22 mm groups did not turn out to be UPT positive. Figure 1 shows a graph which depicts an inverted U-shaped relationship between the MFD among the outcomes of IUI.

**Table 4- Association of Conception rate (UPT positive) with Mean Follicular Diameter (MFD) in combined study groups**

UPT positive	MFD ≤18 mm and >22 mm N (%)	MFD 18.1-22 mm N (%)	Total N (%)	P value
Yes	0	9 (16.3)	9 (12.3)	0.067
No	18 (100)	46 (83.6)	64 (64 (87.7))	
Total	18 (100)	55 (100)	73 (100)	

Chi-square test;  $p > 0.05$  not significant

Table 4 shows the association of conception rate with MFD. When the 4 study groups were combined and modified into 2 groups (group 1 with MFD ≤18 mm and >22 mm, group 2 with MFD 18.1-22 mm), the conception rate in subjects with MFD 18.1-22 mm was 16.3% with a P value of 0.067 (although not significant).

### DISCUSSION

Intra- Uterine Insemination (IUI) is the simplest method of assisted reproduction as it is inexpensive and easy to perform. Success rate of IUI was determined by different factors. In various studies that has been done chance of pregnancy in infertile couples with ovulation induction and IUI had a significant increase<sup>10,11</sup>.

Two important Ultrasound parameters in IUI cycles are Mean Follicular Diameter (MFD) and endometrial thickness at the time of ovulation trigger<sup>12</sup>. Ovulation usually occurs when follicles size are about 21 to 23 mm, although ovulation may occur when the MFD is between 17 mm and 26 mm<sup>13</sup>. The main objective/ outcome of our study was to study the association of Mean Follicular Diameter (MFD) at ovulation trigger and success of Intrauterine Insemination (IUI). 73 participants during the study period who met the eligibility criteria were studied.

#### **Mean Follicular Diameter (MFD)-**

In this study, Of the 73 who underwent IUI, 9 (12.3%) become pregnant successfully. Our result was similar to the study done by **Fallah Tafti T et al**<sup>14</sup>, they have reported about 14.1% pregnancy rate in IUI cycles. Also, **Seddigheh Esmailzadeh et al**<sup>15</sup>, in their study found an overall pregnancy rate of 15%.

Several studies have been done to assess the appropriate size of follicle at the time of ovulation trigger<sup>9,16-21</sup>. In 2010, **Farhi J et al**<sup>17</sup>, conducted a retrospective study to determine the leading follicle size on the day of ovulation trigger and pregnancy rate in PCOS patients treated with clomiphene citrate. Maximum pregnancy rates were achieved when ovulation trigger was given when the follicle size was 18-22 mm. Pregnancy rate was comparatively lesser when the follicular size was 17 mm and 23 mm (8.8% and 8.8% respectively) and lowest 24 mm size (5.7%).

**Mohammad A. Maher et al**<sup>20</sup>, from 2014-2016, studied the effect of follicular diameter during intrauterine insemination on pregnancy outcomes at the time of ovulation triggering. They collected the data from in Saudi Arabia among 516 IUI cycles. They observed a significant increased pregnancy rates among the study population with gonadotropin stimulated IUI cycles when the optimal follicular diameter was between 19 and 20 mm.

In our study, the average of Mean Follicular Diameter (MFD) among those who conceived (UPT positive) was 19.43 mm. Among the women who conceived (UPT positive), the smallest follicular size at the time of ovulation trigger was 18.269 mm and the largest follicular size was 20.597 mm. The average of MFD in those who did not conceive (UPT negative) was 19.97 mm. Among those who did not conceive (UPT negative), the smallest follicular size was 18.285 mm and the largest follicular size was 21.663 mm. No statistically significant difference in MFD was found between women who conceived and who did not conceive. Similar to the above studies by **Farhi J et al**<sup>17</sup>, and **Mohammad A. Maher et al**<sup>20</sup>, in this study, highest conception rate (16.3%) was achieved when ovulation trigger was given at a follicular size of 18.1-22 mm. All the IUI recipients with MFD  $\leq$ 18 mm and  $>$ 22 mm did not conceive. Although this difference was not statistically significant (p value 0.067), there may be an inverted U-shaped relationship between the Mean Follicular Diameter among the outcomes of IUI. However, the optimal size of the leading follicle for ovulation trigger can be recommended between 18-22 mm.

**LIMITATION-** The study was Hospital based study in a tertiary care setting attached to an apex institute of the country. The results obtained in the study cannot be readily generalised to the recipients of IUI in resource limited settings. The absence of association between MFD and the pregnancy outcome of IUI may be due to the non-linear relationship and lower sample size.

## **CONCLUSION**

Of the 73 undergone IUI, 9 (12.3%) became pregnant successfully. The average of Mean Follicular Diameter (MFD) among those who conceived (UPT positive) was 19.43 mm, and in those who did not conceive (UPT negative), it was 19.97 mm and the result was not found to be statistically significant. In groups with MFD 18.1-20 mm and 20.1-22 mm group, we observed successful pregnancy in 12.3% of the study subjects, whereas all the IUI recipients in the < 18 mm and >22 mm groups did not become pregnant. There may be an inverted U-shaped relationship between the MFD among the outcomes of IUI. However, the optimal MFD can be recommended between 18-22 mm for ovulation trigger with hCG for successful pregnancy outcome.

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