

# Intrauterine insemination outcome with and without ovulation induction treatment

Adeela h H. Hussein \*, Inas T. Ahmed \*\*, Abeer A. Mahmood

## ABSTRACT

**Background:** Infertility is a very common condition affecting approximately 13-14% of couples in the reproductive age. In general population; about 85% of couples have achieved conception within a year. Intrauterine insemination is one of the procedure which have a role in the treatment of infertile couple.

**Objectives:** is to confirm that the use of ovulation induction in the course of intrauterine insemination elevates the pregnancy success rate.

**Method:** This study had been conducted between December 2013 till December 2014 in AL-Elwiyah maternity hospital and AL-Samaraii hospital / Baghdad. On history and clinical examination; the chosen couple had the following criteria; primary infertility for more than one year, no previous IUI trials, husbands with normal seminal fluid analysis, wives in reproductive age group; with regular cycles of 24 - 35 days, body mass index (18-26)kg/m<sup>2</sup>, normal body contour, no galactorrhea nor hirsutism, normal uterine cavity and patent fallopian tubes by hysterosalpingography. Total number of cases is 76; had been divided into two groups who underwent IUI schedule, 38 cases preceded by ovulation induction and the other 38 cases had spontaneous ovulation by showing a single dominant Graffian follicle size of 18 mm measured by daily vaginal ultrasound.

**Results:** During the study period; the total number of married women participated in the study were 76; divided into two groups. The first group contains 38 women who had the inclusion criteria of our research, underwent IUI after follow up and confirmed spontaneous ovulation, the second group included 38 women who also had the same inclusion criteria and underwent IUI after effective ovulation

induction. 5 cases became pregnant while 33 cases didn't conceive, while in the second group with ovulation induction; 12 cases became pregnant while the remaining 26 cases failed to conceive; The overall pregnancy rate was highest (31%) in the group treated with ovulation induction and intrauterine insemination in comparison with the other group which revealed a pregnancy rate of only (13%).

**Conclusion:** For fertile couple in which no recognized cause for her infertility; as for history; clinical examination and investigation are concerned, then combination of ovulation induction with intrauterine insemination is an effective means for achieving pregnancy rate by 31% compared with only 13% pregnancy rate in naturally ovulation cycle.

**Key words:** intrauterine insemination, infertile couple, ovulation.

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Infertility is a very common condition affecting approximately 13-14% of couples in the reproductive age. In general population; about 85% of couples have achieved conception within a year.<sup>(1)</sup> Thirty per cent of all women will become pregnant after 1 month of regular unprotected intercourse. The number of women becoming pregnant in each consecutive month then reduces so that only 10% of couples will not achieve pregnancy after 1 year (5% after 2 years).<sup>(2)</sup> Intrauterine insemination prevents 20% of couples from having to move on to IVF. Advantages of intrauterine insemination are; bypassing vaginal acidity and cervical mucus hostility, short distance by deposition of a well prepared sperms as close as possible to the oocytes, noninvasive and inexpensive.<sup>(3)</sup>

**Methods:** This study had been conducted between December 2013 till December 2014 in AL-

Elwiyah maternity hospital and AL-Samaraii hospital / Baghdad.

On history and clinical examination; the chosen couple had the following criteria; primary infertility for more than one year, no previous IUI trials, husbands with normal seminal fluid analysis, wives in reproductive age group; with regular cycles of 24 - 35 days, body mass index (18-26)kg/m<sup>2</sup>, normal body contour, no galactorrhea nor hirsutism, normal uterine cavity and patent fallopian tubes by hysterosalpingography.

Total number of cases is 76; had been divided into two groups who underwent IUI schedule, 38 cases preceded by ovulation induction and the other 38 cases had spontaneous ovulation by showing a single dominant Graffian follicle size of 18 mm measured by daily vaginal ultrasound. Detailed information from each couple was registered as follows; *History*; Duration of infertility, type of infertility, parity, regularity of the cycle, no previous IUI trial, no

previous gynaecological operation, no chronic medical or drug history. History from the husband obtained including; age, medical, drug and job history, timing of intercourse in relevance to the cycle. General examination; for the wife; examination of the weight, height, secondary sex characters, hirsutism, abdominal mass (if any) and genital tract examination. For the husband; examination was performed by a specialist regarding weight, height, secondary sexual characters and genital tract examination. *Investigations:* Seminal fluid sample was obtained after 2 days abstinence. For the wife; hormonal assay in cycle day 2,3 included (FSH, LH, E2, PRL and testosterone), thyroid function test, Hysterosalpingography, vaginal ultrasound starting with cycle day 9 consecutively, till the single dominant Graffian follicle reaches a size of 18 mm then confirming ovulation by the presence of ruptured dominant Graffian follicle and evidence of free fluid in the pouch of Douglas.

Ovulation induction: Was performed by using Clomiphene citrate (CC) tablet 50 mg 1×1 on day 2 of the cycle for 5 days increasing the dose accordingly till ovulatory cycle is confirmed. During the study 3 cases did not continue the course of induction for unknown cause & had been discarded from the group. From the total 38 cases, 3 of them needed CC in a dose of 1×1, 10 cases needed CC in a dose of 1×2, 20 cases needed CC in a dose of 1×3, 5 cases needed CC in a dose of 2×2. Then following up the cycle by vaginal U/S. Human chorionic gonadotrophin (HCG) 5000 IU was injected once the dominant GF size is satisfactory, then we performed the IUI procedure in IUI laboratory 34 - 36 hrs afterwards.

Semen preparation: Fresh semen is usually produced by masturbation and collected into tube, this is firstly analyzed by high power microscope, the technique used in AL-Samaraii hospital for sperm preparation is so called; the swim up technique:- by adding the culture media (Sperm preparation media of medicult ORIGIO Denmark) which contains (Human albumin solution (HAS), recombinant human insulin, gentamicin sulphate 10 microgram /ml). The standard culture media bottle has 60 ml, which should be used within 7 days, kept in incubator at 37°C during its use; shown in Fig(1)

Media is added to the freshly collected semen sample in a percentage of 1:1 results in improved motility and correct high viscosity of

the semen. Such media which was used is to achieve the largest number of morphologically normal motile spermatozoa in a small volume of physiologically culture medium free from seminal plasma, leukocytes and bacteria. Then the tube which contains the semen and media is washed by centrifugation at 2000 rounds per minute for 10 minutes as in Fig(2).

The next step will be aspiration of the supernatant layer which contains plasma and oxidants to be thrown away, using Pasteur pipette. The remainder (precipitate) contains sperm in high concentration is added by another 0.5 ml of same media Fig(3) and put in oblique position (to increase the surface area of interfacing between media and sperms) in incubator at 37°C for 30 minutes Fig(4). After that aspirate (by Pasteur pipette) the superior and medium layer of specimen and put it in a new tube and examine under high power microscope. The preferred sample is the one that contains >1 million of normal morphology motile sperms then skip to the next step; insemination as rapidly as possible as the delay decrease the adenosine triphosphate (ATP) amount in sperms. Timing of insemination is performed at 36 hours after HCG injection observed by serial ultrasound.

Insemination should be carried out using aseptic technique to avoid the risk of infection without using antiseptic material and gently to avoid traumatizing the endometrium as this could induce cramping and bleeding that may adversely affect the survival of the spermatozoa. The procedure is performed in lithotomy position; the cervix is exposed by Cusco's speculum and cleaned. The volume of prepared semen sample should not exceed >0.4 ml then withdrawn using a syringe attached to an IUI catheter (GYNETICS-Belgium) as in Fig(5). The catheter is threaded into the uterine cavity, just passing the cervix and semen is gently injected, the catheter is withdrawn slowly pressing on the syringe, the woman is advised to rest in place for 30 min.

The usual luteal support for IUI in AL-Samaraii Hospital is either oral progesterone Dydrogestrone (Duphastone) tab 10 mg 1×2 for 2 weeks or vaginal gel micronized progesterone (Crinone) 1×1 for 2 weeks.

Follow up is by measurement of B-HCG level two weeks after insemination.



Figure 1: sperm preparation media ORIGIO Denmark



Figure 2: centrifugation.



Figure 3: 0.5 ml of media added to the precipitate



Figure 4: the oblique way of putting the prepared sample in incubator in 30 minute



Figure 5: GYNETICS-Belgium catheter for inseminating prepared sample

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**Results:**In current study, total number of married women participated in the study were 76; divided into two groups, as shown in Table (1). The first group contains 38 women who had the inclusion criteria of our research, underwent IUI after follow up and confirmed spontaneous ovulation, the second group included 38 women who also had the same inclusion criteria and underwent IUI after effective ovulation induction.

Successful IUI was confirmed by a positive pregnancy test in form of B-HCG test to both groups, 2 weeks after IUI procedure.

In the first group with spontaneous ovulation; 5 cases became pregnant while 33 cases didn't conceive, while in the second group with ovulation induction; 12 cases became pregnant while the remaining 26 cases failed to conceive;this means that the overall pregnancy

rate was highest in those treated with ovulation induction and intrauterine insemination as in Table (2).

The overall pregnancy rate was highest(31%) in the group treated with ovulation induction and intrauterine insemination in comparison with the other group which revealed a pregnancy rate of only (13%) as in Table (3).

So the predictive value of pregnancy in the group where IUI was done after ovulation induction was higher than that where IUI was done after spontaneous ovulation; as shown in Table (4).

Positive predictive value is 70% of the current study and that is considered as a significant result.

Table 1: Number of cases with and without ovulation induction

Total No.	76 cases	Percent %
No. of cases with spontaneous ovulation	38	50%
No. of cases with ovulation induction	38	50%

Table-2- B-HCG results of all cases in current study

B-HCG	Spontaneous ovulation	Ovulation induction	Total	Percentage Rate
+ve	5	12	17	22.3%
-ve	33	26	59	77.6%

**Table (3) Pregnancy rates statistic**

Type of ovulation	Pregnancy rates
Spontaneous ovulation	13%
Ovulation induction	31%

**Table (4) Statistical values of the studied groups**

Sensitivity	Specificity	Positive predictive value	Negative predictive value
31%	86%	70%	55%

**Discussion:** Though thirty per cent of all women will become pregnant after 1 month of regular unprotected intercourse<sup>(2)</sup>, the assisted reproductive technology (ART) has improved dramatically in the past 20 years<sup>(4)</sup>. Nevertheless, many patients undergoing ART respond poorly to gonadotropins and continue to yield limited overall success<sup>(5,6,7,8,9,10)</sup>. Intra uterine insemination (IUI) is the best first line treatment and the most effective procedure for unexplained and male factor subfertility<sup>(11)</sup>. Several studies had suggested that IUI cycles with ovarian stimulation improves the probability of conception in couples with unexplained infertility but the main concern is the efficacy of the agent which has been used for stimulation<sup>(12)</sup>. The majority of infertile couples seek a less invasive and less costly therapeutic option in assisted reproductive techniques (ART); intrauterine insemination (IUI) is one of these options. The etiology of infertility is important to achieve remarkable IUI success. Favorable variables for treatment success are as follows: age <40, duration of infertility ≤5 years and a cause of infertility<sup>(12)</sup>.

Success rates of around 5% per cycle have been quoted for unstimulated IUI, increasing to 8-10% for stimulation with Clomiphene citrate. Although success rates of 35% have been quoted in the literature, these tend to be highly selective series<sup>(13)</sup>.

In current study, comparison was done between two groups with and without ovulation induction underwent IUI, 38 cases underwent IUI with spontaneous ovulation; 5 cases became pregnant (13%) in comparison with 12 cases out of 38 cases became pregnant (31%) and had ovulation induction by Clomiphene citrate which is

well tolerable, with less complications and less expensive. Ovulation induction increases the number of mature follicles which explain high chance of pregnancy; this is confirmed by a research of Gómez-Palomares 2008 who showed a clinical pregnancy rate more statistically significant in the group treated with GnRH with IUI than control group, this indicates that IUI with other methods of ovulation induction increase chance of pregnancy and this goes with our study<sup>(14)</sup>. A metaanalysis of Shan Luo research 2014 has shown that GnRH used in controlled ovarian stimulation cycles with IUI can significantly increase the clinical pregnancy rate<sup>(15)</sup>. In Pavone M. research 2013 concluded that Aromatase inhibitors may be an effective alternative treatment to clomiphene citrate for both ovulation induction and superovulation attributed to antiestrogenic effects of clomiphene on cervical mucus and the endometrium<sup>(16)</sup>, while other researches as by Mohamed A Bedaiwy 2011 shows multifollicular development and better pregnancy outcomes in IUI cycles with the use of ovulation induction drugs as letrozole 2.5 mg/day on cycle days 3 to 7 in a group of patients suffering unexplained infertility (11.89 %) comparing to control group with naturally ovulation cycle (4.8 %) while in our study pregnancy rate with CC was higher than this study because Letrozole results in some minor changes in follicular, hormonal and endometrial dynamics<sup>(17)</sup>. In Bhattacharya S research 2008 concluded that; in couples with unexplained infertility existing treatments such as empirical clomiphene and unstimulated intrauterine insemination are unlikely to offer superior live birth rates compared with expectant

management as the pregnancy rate with oral CC (14%) and in unstimulated IUI was (23%)<sup>(18)</sup>.

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