

Outcome of In-Vitro Fertilization in the First Government Set-up Fertility Center of Bangladesh

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Abstract

Introduction: Infertility as a global health issue is very much attended by the health sectors of most of the developed countries of the world. It remains as a neglected issue in Bangladesh's reproductive health policy as emphasis is always been on the problem of overpopulation. Bangladesh Armed Forces have come forward to establish the first government set-up Artificial Reproductive Technology (ART) center to help the infertile couples of Bangladesh.

Aim: To assess the outcome of in-vitro fertilization (IVF) procedures in relation to different demographic characteristics of the patients getting treatment at Fertility center, combined military hospital (CMH), Dhaka.

Methods: Out of more than thousand patients, 46 couples were selected for IVF cycle scheduled to be held on the month of July 2017 and October 2017. Each selected female and male patient had a normal basic fertility work up. In both batches, female factors were predominant. Male factor and combined factors were also present. Data were collected prospectively using a data collection sheet over the period of one year starting from July 2017 to June 2018 to observe the last patient upto the delivery of her offspring.

Results: A total of 46 couples or 92 patients were treated for infertility. Out of 46 female patients, most (about 40%) were within the range of 26 to 30 years of age. About two-thirds patients had primary subfertility. Most common cause of infertility of female partners was the tubal cause (52%) and of male partners was severe oligozoospermia (47%). A procedure of IVF like conventional IVF was done in 64% and Intra Cytoplasmic Sperm Injection (ICSI) in the remaining. Embryo transfer was performed in 30 patients. The embryos of 13 (33%) patients were cryopreserved in both batches. Rate of retrieved oocytes ranged from 3 to 29 in the 1st batch and for the 2nd batch it was from 1 to 17. Pregnancy rate was 80% in first batch, but in the second batch it was only 33%. Abortion rate was also very high (80%) in the second batch.

Conclusion: In fact, infertility has become a burning health issue to the sufferers of fertility problems as well as career-oriented

generation of this century and the society seeks the remedy to help them. Like the Fertility Center, CMH, Dhaka other government set up centers should come up to provide facilities that enables the women having the dream of motherhood true.

Key-words: Infertility, In vitro fertilization (IVF), Artificial Reproductive Technology (ART), Intra Cytoplasmic Sperm Injection (ICSI), Embryo transfer, cryopreservation.

Introduction

The clinical definition of infertility provided by world health organization (WHO) is a disease of the reproductive system characterized by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse¹. In an average 15% of couples are infertile worldwide which ranges from 8% to 12% and in some areas that figure reaches one-third or more of couples^{1,2}. According to WHO data more than 180 million couples in developing countries suffer from some sorts of infertility¹. According to Center for Disease Control (CDC) 1.5 million women in the US (6%) are infertile³. One study has shown that the prevalence of primary infertility in developed and less developed countries ranges from 6.6-26.4% and 5-25.7% respectively⁴.

The universal desire to have a child is the ultimate goal of life of each species. In fact, human existence reaches completeness through procreation of child and inability to fulfill this dream affects mental, physical and social health and sometimes it leads to divorce in many developing countries like ours^{5,6}. With advancement of time and technology, both male and female are career oriented, resulting into advanced age of marriage, diminished reserve, and many other causes that lead the couples to depend on assisted reproduction⁷. Assisted reproduction technology (ART) includes all the methods used for fertilization, which is not achieved through sexual intercourse⁸. It involves hormonally controlled ovulatory process, removing ova (eggs) from the woman's ovaries and fertilizing with husband's sperm outside the human body. The resulted embryo is then transferred to the patient's uterus with the goal of establishing a successful pregnancy. Failure may occur at multiple points of In Vitro Fertilization (IVF) cycle starting from failed fertilization, failed implantation, early fetal loss due to decrease of raised-human Chorionic Gonadotropin (hCG) level to spontaneous abortion, IUD etc⁹.

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Infertility as a global health issue is very much attended by the health sectors of most of the developed countries of the world. It is a burning issue in Bangladesh's reproductive health policy as emphasis is always been on the problem of overpopulation¹⁰. So, in Bangladesh, no such epidemiological study has been conducted to assess the real estimate of infertile population at national level. A global review of infertility from the World Fertility Survey and others estimated infertility rates of South Asian countries is 4% in Bangladesh and of overall primary and secondary infertility in South Asia is 15% in Bangladesh^{11,12}. Bangladesh Armed Forces has come forward to establish the first government set-up Artificial Reproductive Technology (ART) center to help the infertile couples of the country. Many female persons are enrolled each year. Like the male counterpart, female population of Bangladesh has become more career-oriented now-a-days. Study revealed that the prevalence of primary infertility in developed and less developed countries are 6.6-26.4% and 5-25.7% respectively^{13,14}. As in civil counterpart, infertile patients in Bangladesh Armed Forces are also increasing rather more in number for special of job pattern. For Job pattern, from the very beginning of their married life, many of them cannot stay with partner continuously. Nevertheless many male and female members of armed forces may suffer from gradual decrease of reproductive capability due to strenuous physical exercise, tight garments, prolonged standing¹⁵.

IVF service in Bangladesh was so far confined to some private centers only. This center is the first functioning Government set-up center of Bangladesh and practices such as sperm or oocyte donation and surrogacy are not allowed¹⁶. The aim of this study was to assess the outcome of IVF procedures in relation to different demographic characteristics of the patients getting treatment at Fertility center, CMH, Dhaka.

Materials and Methods

This prospective cohort study was conducted in the Fertility Center, Combined Military Hospital, Dhaka from July 2017 to June 2018. Purposively 46 couples selected for IVF in first two batches were included in this study out of more than one thousand patients reported for different types of infertility were screened, investigated thoroughly and excluded depending on exclusion criteria. The included 46 patients were followed up time to time from their enrollment in the IVF cycle till the delivery of the last baby of 2nd batch. Out of them 23 patients were selected for first batch and 23 patients were selected for 2nd batch of IVF cycles which were scheduled to be held on the month of July 2017 and October of 2017. Each selected female patient had a normal basic fertility work up including baseline ultrasonogram, sonosalpingography, hysterosalpingo- graphy or laparoscopy in most.

For cycle synchronization before each IVF cycle, all patients were kept on oral contraceptive pill to bring them at or near the same date of LMP. Then, a standardized protocol, namely long luteal-phase pituitary down-regulation using the GnRH analogue

Leuprolide from the day of 21 of the current menstrual cycle was started for all patients. On day two of the cycle following Leuprolide acetate administration LH, Estradiol were evaluated and AFC (antral follicular count) was done by TVS (transvaginal sonography) for each patient. Ovarian stimulation started with Follicle Stimulating Hormone or Human Menopausal Gonadotropin according to patient status. The dose of Gonadotropin was adjusted according to day-2 basal hormone evaluation, age, BMI, AMH and previous history of response to gonadotropin. When at least three or four follicles reached a mean diameter of 17 or 18 mm, 5000/10,000 IU of hCG or 250 microgram Ovidrel was administered and after 34-36 hrs, TVS guided oocyte retrieval was performed under total intravenous anaesthesia^{17,18}. Conventional IVF was done in 14(63.6%) patients in 1st batch and 11(57.9%) patients in 2nd batch and ICSI was done in 7(31.8%) patients in first batch and also 7(38.9%) patients in 2nd batch.

All fresh embryo transfers were done on 3rd day after retrieval (D-2 embryo). 2-5 good quality (grade I/II) embryos were transferred according to SART criteria^{17,18} and in the 2nd batch, only one grade I embryo developed in each 5 patients, and were transferred in the fresh cycle. After 18 days of embryo transfer serum β -hCG was requested and pregnant women had an ultrasound scan on day 21 if biochemical pregnancy was positive. If fetal pole and positive fetal heart sound were demonstrated, clinical pregnancy was confirmed. For 1st batch, biochemical pregnancy was 12 and in 2nd batch it was 5.

Data were collected prospectively using a data collection sheet over the period of one year starting from 17 July 2017 to 18 June 2017. Ethical clearance was taken from ethical committee of CMH Dhaka. Funding was private. Data were collected, compiled and analyzed. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) software (version 23.0).

Results

Patients of 1st and 2nd batch were matched according to their age, BMI, type of infertility and indications for IVF. A total of 46 patients were selected for consecutive two batches. Out of them, about 13% were below 25 years of age and also 13% were older than 36 years. But most of the patients (about 40%) were within the range of 26 to 30 years of age. About two-thirds patients had primary subfertility. Most common cause of infertility of female partners was the tubal cause (52%) and of male partners was severe oligozoospermia (47%) (Table-I). Total distribution of male, female and combined causes of infertility selected for ART in first two batches are shown in Figure-1.

Table-II shows the procedures performed in both batches. For first batch one patient was cancelled for hypersensitivity reaction and during ovum pick up (OPU) no oocyte could be retrieved due to such reaction. For the second batch one patient was cancelled few days before OPU due to non development of follicles. Regarding 3 cases of 2nd batch, no oocyte could be collected

during OPU probably due to empty follicular syndrome and no sperm could be collected from the only azoospermic patient of this batch. So in vitro fertilization procedure, by conventional IVF or ICSI, could be done in 22 cases in 1st batch and 18 cases in 2nd batch. Out of these 40 patients, conventional IVF was done for 25 (64%) patients and ICSI was done for 15 (37%) patients. ICSI was specially done by ejaculated sperm in severe oligozoospermia patients and by TESA sample for azoospermic patients. Embryo transfer was performed in 30 patients. Out of them 3 frozen transfer were performed in second batch only. The embryos of 13 (33%) patients were cryopreserved. Table-III shows the laboratory data of both batch. Cycle cancellation rate was only about 4% in

1st batch, but it is about 22% in second batch. Total 304 oocytes were collected, from each patient on an average (13±8.1) oocytes ranging from 3 to 29 in the 1st batch. But in the 2nd batch total 112 oocytes (5±4.6) were retrieved from each patient ranging from 1 to 17. For one couple, due to unavailability of sperm from husband, all oocytes (10) were cryopreserved. Table-IV summarizes that pregnancy rate was 80% in first batch, but in the second batch it is only 33%. Abortion rate was also very high (80%) in the second batch. Ectopic pregnancy and multiple pregnancies were present only in first batch. Pregnancy rate was highest in both batches between the age group of 26 to 30 years.

Table-I: Demographic data of infertile couple

Characteristics		Number of patients	
		1 st batch, n (%)	2 nd batch, n (%)
Women's age (years)	20-25	03 (13.0)	03 (13.0)
	26-30	09 (39.1)	10 (43.5)
	31-35	08 (34.8)	05 (21.7)
	36-40	03 (13.0)	05 (21.7)
Mean ± SD; BMI (kg/m ²)		27.1 ± 2.9	26.3±2.9
Female cause of infertility	Tubal cause	12 (52.2)	07 (30.4)
	Polycystic ovary syndrome	07 (30.4)	02 (8.7)
	Poor ovarian reserve	-	04(17.4)
	Recurrent pregnancy loss	-	01(4.34)
	Endometriosis	02 (8.7)	07(30.4)
	Endometrial factor	-	02(8.7)
Male cause of infertility	Azoospermia	01(4.3)	01(4.3)
	Severe oligozoospermia	11(47.8)	06 (26.1)
Infertility type	Primary	16 (69.6)	13 (56.5)
	Secondary	07 (30.4)	10 (43.5)

Table-II: Procedures performed for ART

Name of Procedure	1 ST batch (n=23)	2 ND batch (n=23)
Ovum Pick Up (OPU)	23/23	22/23
Conventional In vitro fertilization (CIVF)	14/22 (63.6%)	11/18 (57.9%)
Intra Cytoplasmic Sperm Injection (ICSI)	07/22 (31.8%)	07/18 (38.9%)
Percutaneous Epididymal Sperm Aspiration (PESA)	--	01
Testicular Epididymal Sperm Aspiration (TESA)	03	01
Embryo Transfer	15/22	12+3/18+3
Cryopreservation	07/22	06/18

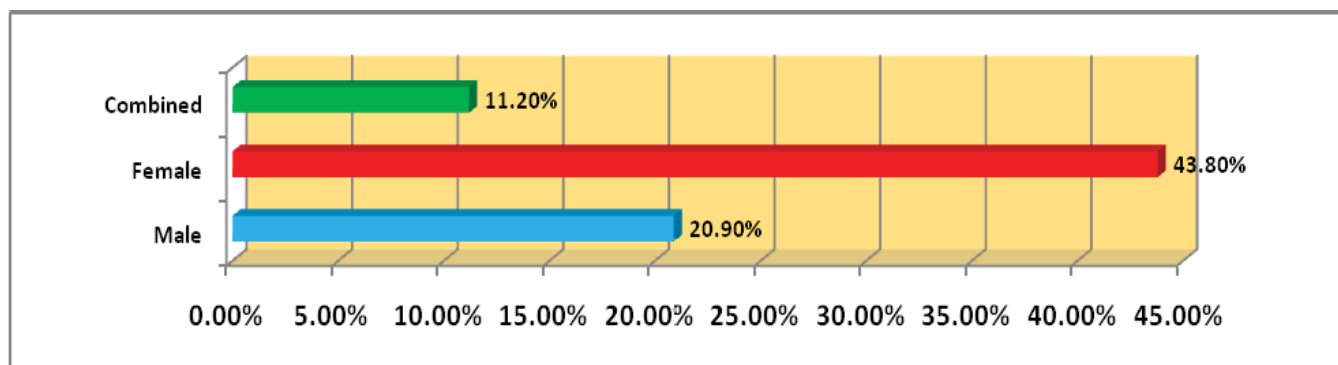


Figure-1: Percentage of causes of infertility

Table-III: Table-III: Laboratory data

Variables	1 st batch (n=23)	2 nd batch (n=23)
Number of patients	23	23
Cycle cancellation rate	1/23 (4.3%)	5/23 (21.7%)
Number of oocytes retrieved (mean±SD)	304 (13±8.1)	112(5±4.6)
Number of embryos transferred (mean±SD)	48 (3±1.0)	28 (2±1.3)
Fresh transfer cycle rate	15/22 (68.2%)	12/18 (66.7%)
Frozen transfer cycle rate	0	03

Table-IV: Pregnancy rate and outcome

Variables	1 st batch (n=23)	2 nd batch (n=23)
Pregnancy rate	12/15 (80%)	05/15 (33.3%)
Abortion rate	05/12 (41.7%)	04/05 (80%)
Ectopic pregnancy rate	03/12 (25%)	--
Multiple pregnancy rate	02/12 (16%)	---
Take home baby rate	04/12 (33.3%)	01/05 (20%)
Perinatal death rate	01/12 (8.3%)	--

Discussion

Infertility remains an ignored issue in Bangladesh's reproductive health policy; as being an overpopulated country the emphasis has always been on the control of population problem¹⁰. Infertility affects both men and women, yet women particularly in developing countries like ours, have to bear the sole blame for barren marriage¹², even in many cases the husbands do not agree to go for any investigation also. So a very few percentage of the affected population of Bangladesh is getting treatment. This prospective study was designed to assess the demographic characteristics and outcome data from couples seeking IVF treatment in a newly established first government set up IVF center of Bangladesh, Fertility center, CMH, Dhaka during the period starting from controlled ovarian hyperstimulation of the women to the birth of the last baby of mother who was included in this study. Results of this study shows woman's age, BMI, cause of infertility of partners with the outcome of IVF treatment. Most of these results have resemblance with studies done previously on this topic elsewhere in the world¹⁹⁻²¹.

This study shows that the main portion (about 55%) of female patients seeking IVF treatment is within 20 to 30 years age group. It is similar to the study of Roupa et al⁸ in 2009 which was about 65%. It disagrees with Bodri D et al²¹ who shows that patients reporting at their center for IVF treatment are mainly above the age of 38 years. This may be due to geographical variation where age of marriage is in early age as that of our country and in others which differ may be due to late age of marriage or delaying in planning for pregnancy. It is now common due to increasing carrier and job involvement of both male and female partners resulting in delay in reporting for infertility treatment. With the advancement of female age, fertility rate is decreased²⁰. Our study shows similar result where pregnancy rate is decreased after 37 years of age. In his study Qublan et al showed mentioning

agreement with his referred reported data that IVF outcome becomes poorer with the advancement of age significantly after the age of 37 years as ovarian reserve, endometrial receptivity and egg quality all these factors become impaired with increasing age^{20,21}. This study also shows that the mean body mass index (BMI) is about 27±2.8 kg/m² for the female patients which is remarkably higher than study of Bodri D et al²¹ where it is 20.8 ± 2.7 kg/m² in Bangladesh specially the female partner of infertile couples are shy and they are reluctant to do outdoor activities and exercises. Again most of the endocrine cause is PCOS and in this study the number of PCOS patients is also not very less (20%). PCOS and advanced female age are the main cause of increased BMI in this study.

According to this study, tubal cause contributes maximum female patients reported for IVF treatment to Fertility center, CMH Dhaka. This result is also supported by previous studie^{8,20}. But the second cause varied with the studies^{8,21} where they showed the unexplained cause of infertility as the second female cause of infertility. This study disagrees with this as we find endometriosis as a second dominant female cause. Unexplained infertility accounts 25-30% of female infertility and it is the second common causes of infertility but our patients were selected depending on their absolute need of IVF among all participants. Stage III and IV endometriosis were more in this study. This study also highlights the male cause of infertility where severe oligozoospermia occupies a wide area. As gamete donation or surrogacy is not accepted here, so patients of azoospermia or severe oligozoospermia have no options if surgical retrieval is failed. This happens to one case in second batch and oocytes of female partner were cryopreserved. No supporting evidence could be collected for such situation as almost all of the IVF centers are working with sperm donations and it is an important means of their success.

The range of oocyte retrieval from the patients was from 3 to 29

in the first batch and from 1 to 17 in the second batch. The resulting pregnancies are more positive in those within the range of 4 to 12 oocytes. This data agrees with Qublan et al and Bodri D^{20,21}. Embryo transfer (ET) is the climax of a long series of arduous laboratory and clinical protocols involved in ART. In fact, it is the knowledge and skill of clinician as well as embryologist which are very much required for the success of this procedure¹⁸. In the first batch Fresh cycle embryo transfer (ET) was done in 15 patients out of 22, whose embryos developed²². For the remaining 7 patients embryos were frozen for future as their situation were not favorable for transfer. Out of these 7, for 3 female partners frozen cycle embryo transfer was done along with the 12 fresh cycle embryo transfer patients of second batch. IVF increases the risk of multiple births about 25% in UK and multiple pregnancies statistically increases rate of preterm birth and perinatal death²³. This study shows a nearly similar but much lower rate. A government set-up institution has a number of limitations that does not allow it to work focusing only on outcome. No national IVF policies (restriction and liberations) for individual treatment strategies in IVF clinics have yet been established by Bangladesh Government, but very few IVF clinics of private sector are following the international policies. As a new center the size of study population is relatively small which affects the outcome data sometimes.

Conclusion

Since from the ancient period of time man is moving science and science is moving man. It is the mercy of science that is able to fulfill the long desired expectation of infertile couples. Globally the management of infertility has gone a long way. We are also developing keeping pace with them. And it is time when we are capable enough to treat infertile couples in our very own country. In fact, infertility has become a burning health issue to the sufferers of fertility problems as well as career-oriented generation of this century and the society seeks the remedy to help this population. Like the Fertility Center, CMH Dhaka other government set up centers should come up to provide facilities that enable the women having the dream of motherhood true.

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