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The Outcome of Assisted Reproductive Techniques among Couples with Male Factors at Prince Khalid Bin Sultan Fertility Centre, Kingdom of Saudi Arabia

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Abstract

BACKGROUND: Thirty-three percent of infertility due to paternal factors, there are an increasing proportion of couples who decide to conceive by assisted reproductive techniques (ART). The outcome prediction is pivotal for decision making.

AIM: We aimed to study the pregnancy outcomes of different ART with male factors infertility.

METHODS: This retrospective cross-sectional study conducted at Tabuk, Kingdom of Saudi Arabia. One hundred fifteen patients' records reviewed using a structured checklist to collect demographic data, sperm (concentration, motility, and morphology). Female with significant infertility factor were excluded. Chi-square was used for the outcome of various ART.

RESULTS: Out of 115 couples with male factors; treated by Intracytoplasmic Sperm Injection (ICSI), In Vitro Fertilization (IVF) and Intrauterine Insemination (IUI); the mean age was 35.2 ± 6.3 years for men and 29.7 ± 5.1 for females. IVF had the highest success rate overall and had a high pregnancy rate with oligospermia and asthenospermia. ICSI has a good outcome for those with azoospermia, severe oligospermia, and teratozoospermia. IUI must be tried as a first line treatment when semen concentration is more than 10 million sperm/ml. all are not significant (P > 0.05).

CONCLUSION: No significant differences were reported in the pregnancy outcome between various assisted reproductive techniques, smoking, type of infertility and medication.

Introduction

Infertility is a serious health problem in the Kingdom of Saudi Arabia; it accounts for 19% in some regions [1]. More than half million couples are waiting for assisted reproductive technology. Male factor infertility is a term that means the problem in couples is due to a male partner. Only a limited number of men with primary male factor infertility have potentially treatable conditions. However, assisted reproductive techniques (ART) are more hopeful than any other treatment option. Little information is available regarding male factor infertility and its treatment in the Kingdom of Saudi Arabia; we found a single study published by (Haifa et al.), it indicated that abnormal semen parameters were present in 47% of men attending infertility clinic [2], whereas worldwide it accounts for one-third of cases of infertility [3].

Semen analysis is the first step in investigating male factor infertility. It is a simple and a useful test up to now. The World Health Organization (WHO) classification for male factors infertility was based on a variety of sperm disorders in which the cut-off values are; sperm concentration 15 million sperm/ml (oligospermia), total sperm motility 40% (asthenospermia) and normal forms 4% (teratozoospermia) [4]. There is little agreement about the best predictor of pregnancy outcome in various seminal abnormalities. Data suggest that IUI improves pregnancy rates in couples with mild oligospermia (10-15 million sperm/ml) [5, 6]. IVF was used for the

treatment of male infertility in patients with moderate oligospermia (5-10 million sperm/ml). However, in severe oligospermia (< 5 million sperm/ml) and poor sperm motility, the fertilization rate of the oocytes was much less [7, 8]. Intracytoplasmic Sperm Injection (ICSI) has revolutionalized the treatment and improved the prognosis for infertile men with very severe oligospermia, asthenospermia, teratozoospermia, and even azoospermia [9, 10].

Although Male infertility is a universal health issue, and it is important to understand its aetiology and treatment, it is understudied in the kingdom of Saudi Arabia. The literature regarding the best method of assisted reproductive technology for male factor infertility is scarce, to our best of knowledge, this is the first study to address this important issue in Tabuk City.

Thus we conducted this research to evaluate the outcomes of different assisted reproductive technology (IUI, IVF, and ICSI) in couple with male factor infertility.

Subjects and Methods

A cross-sectional descriptive, longitudinal, hospital-based study was conducted from May 2012 to May 2014. All patients who underwent different types of assisted reproductive techniques (IUI, IVF or ICSI) for male factor infertility at Prince Khalid bin Sultan Fertility Centre in King Salman Armed Force Hospital was included. This centre was randomly chosen from the three centres in Tabuk City.

The records of one hundred and fifteen patients were reviewed. Inclusion Criteria were: infertile male partner due to seminal abnormalities. Significant female factor infertility contributing to the couple's infertility and couples unsuitable for IUI, IVF or ICSI were excluded. The patient's privacy was ensured during data collection. A structured checklist was used to collect the following parameters: Demographic data, sperm concentration, sperm motility, and sperm morphology. The cycles with embryo transfer were considered. All the males were soldiers. Then comparisons were undertaken between the above mentioned seminal parameters in the patient with male factors infertility and the outcome of various assisted reproductive techniques

For this research the following definitions were adopted:

1) Assisted reproductive technology (ART): Describes clinical and laboratory techniques used to achieve pregnancy in infertile couples [11].

2) Intrauterine insemination (IUI): Is the first therapeutic step in assisted reproductive techniques, and is especially appropriate for cases with mild male factor infertility, anovulation, endometriosis with at least one patent tube, and unexplained infertility [12].This technique uses a thin flexible catheter to place a prepared semen sample into the uterine cavity transcervical near the anticipated time of ovulation with or without superovulation.

3) In vitro fertilization (IVF): Mature oocytes from stimulated ovaries are retrieved transvaginally with ultrasound, and then fertilization in the laboratory ("in vitro") will be undertaken, after which, one or more of the embryos are transferred transcervical into the uterine cavity using ultrasound guidance.

4) Intracytoplasmic sperm injection (ICSI): This variation of IVF is most applicable to male factor infertility. During this technique, cumulus cells surrounding an ovum are enzymatically digested, and a single sperm is directly injected into the cytoplasm of a mature oocyte [13].

5) Mild oligospermia (10-15 million sperm/ml), Moderate (5 - 10 million sperm/ml) and severe (< 5 million sperm/ml) [5, 6].

Ethical considerations

The ethical committees of both the University of Tabuk and King Salman Armed Force Hospital approved the research. The collected data were approached confidentially and were used only for research. Data were analysed by using the Statistical Package for Social Sciences software (SPSS version 20). The chi-square was used for testing the statistical significance, data were presented as percentages or mean ± SD, and a P-value < 0.05 was considered as statistically significant.

Results

Out of 115 couples with male factor infertility, the male and females ages were 35.2 ± 6.3 and 29.7 ± 5.1 years respectively. The mean duration of infertility was 6.5 ± 4.2 years; sperm concentration was 12.1 ± 6.4 million/ml, total sperm motility was 25.6 ± 23.8 while normal sperm form constituted 15.8 ± 13.6 (Table 1).

Table 1: Basic characteristics of the study group (n = 115)

Character	Mean ± SD
Husband age	35.2 ± 6.3
Wife age	29.7 ± 5.1
Duration of infertility (years)	6.5 ± 4.2
Sperm concentration (millions)	12.1 ± 6.4
Total sperm motility%	25.6 ± 23.8
Normal sperm form	15.8 ± 13.6

The overall pregnancy rate in different Assisted Reproductive Technology was reported to be 46.4% for IVF compared to ICSI and IUI which are 35.5 and 16% respectively (P = 0.061).

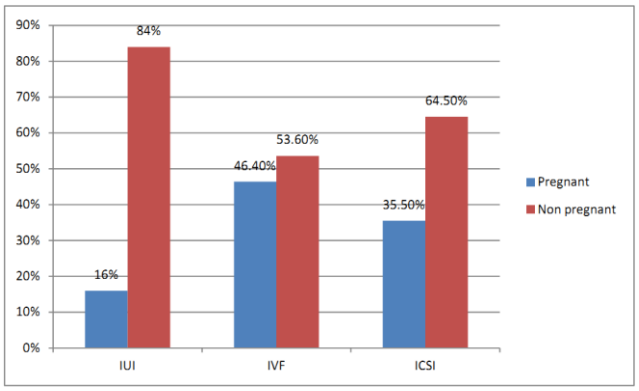

Figure 1: Outcome in the different types of Assisted Reproductive Technology (n = 115)

Figure 2 illustrated the outcome in ICSI with azoospermic patients (pregnancy rate of 36.7%).

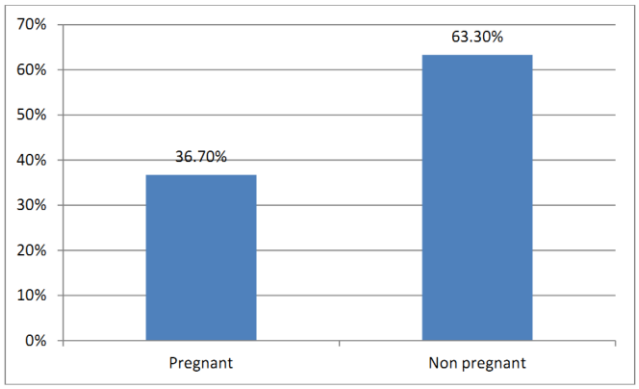

Figure 2: Outcome of ICSI in patient with azoospermia (n = 30)

The outcome of a different semen concentration showed that ICSI is more efficient (pregnancy rate 24.2%) than the other methods when the level below 5 million sperm/ml. In the patients of IUI group, there is no pregnancy when the concentration is below ten million sperm/ml (Table 2).

Table 2: Pregnancy rate according to different semen concentration

Semen concentration (million sperm/ml)	Pregnant rate%		
	ICSI (n = 62)	IVF (n = 28)	IUI (n = 25)
<5	24.2%	7.1%	0
5-10	1.6%	10.7%	
0			
10-15	6.5%	14.3%	8%
>15	3.2%	14.3%	8%

Table 3 illustrated the pregnancy rates among male partners with oligospermia in which the outcome was 47.8%, 36.4% and 20% in IVF, ICSI, and IUI respectively, with no significant statistical difference (P value = 0.304). The pregnancy rate of male partners with asthenospermia in IVF, ICSI, and IUI was 53.8%, 32.0%, and 13.3% respectively. There was no significant difference (P value = 0.072). Males with teratozoospermia only gets pregnant by ICSI in which pregnancy rate was 60% but not statistically significant (P value = 0.387). The pregnancy rate was 30.4% in smokers and 34.7% in nonsmokers with no significant statistical difference (P value = 0.808). Pregnancy rate was 43.9% among women with secondary infertility vs. 28.3% in those with primary infertility (P value = 0.104). The highest rate of gestation was reported among females taking Menogon 43.5% followed by Gonal-f 32.5%, then Fostimon and Clomid which were 25.0% with no significant statistical differences (P value = 0.697).

Table 3: Assisted Reproductive Technology outcome about various factors

Character		Pregnant%	Non-pregnant %	P-value*
Males with oligospermia (n = 88)	ICSI	36.4%	63.6%	0.304
	IVF	47.8%	52.2%	
	IUI	20%	80%	
Males with asthenospermia (n = 78)	ICSI	32.0%	68.0%	0.072
	IVF	53.8%	46.2%	
	IUI	13.3%	86.7%	
Males with teratospermia (n = 38)	ICSI	60%	40%	0.387
	IVF	0	100%	
	IUI	0	100%	
Smoking: (n = 115)	Yes	30.4%	13.9%	0.808
	No	34.7%	52.2%	
Type of infertility: (n = 115)	Primary	28.3%	71.7%	0.104
	Secondary	43.9%	56.1%	
Medications of ovulation induction: (n = 115)	Menogon	43.5%	56.5%	0.697
	Gonal-f	32.5%	67.5%	
	Fostimon	25.0%	75.0%	
	Clomid	25.0%	75.0%	

Discussion

In the present study, retrospectively 115 couples with male factor problems were recruited, and the woman had no identifiable infertility factor to make the differences in sperm parameters more significant. ART has become widespread treatments for alleviating male factor infertility, Different methods (IUI, IVF, and ICSI) are recommended, and the pregnancy rate depends mainly on sperm parameters such as sperm concentration, motility and morphology [14]. There is a positive correlation between sperm concentration and pregnancy [5].

The current data showed no statistical difference between various seminal abnormalities and pregnancy outcomes, the overall reported pregnancy rates were higher in IVF followed by ICSI and then IUI (46.4%, 35.5%, and 16% respectively) but there is no significant statistical difference between various methods P=0.061. In contradictory to Kastrop PM et al. [15] concluded that ICSI appeared to be far better to IVF attempt. When using IUI the present findings, 16% were more or less similar compared to Allen et al. who observed pregnancy rates between 8% and 22% [16].

In this study, pregnancy was achieved when

sperm concentration was above 10 million/ml when using IUI. The lowest pregnancy rate achieved through IUI with oligospermia and asthenospermia (20% and 13.3%) but these values are acceptable when IUI is considered as a first-line treatment because it is simple, cost-effective and less invasive treatment option forms of assisted reproduction [17]. Cohlen BJ. State that a significant increase in pregnancy rates after IUI compared to timed intercourse in an infertile male [18]. For this reasons, it must be attempted in these groups of patients before proceeding to more expensive and invasive methods such as IVF or ICSI [19].

IVF was introduced as a treatment for tubal infertility; it quickly became apparent that it was also an excellent option for male subfertility. In the current study IVF had a higher pregnancy rate than the others in cases of oligospermia and asthenospermia which were 47.8%, and 53.8%, respectively. ICSI success rate was lower 36.4% and 32.0% with the same sperm abnormalities but these results with no significant difference. From these results for all the above three modalities of treatment, IVF had a higher success rate in our centre. The use of ICSI as the first option for all cases of male factor infertility becomes a routine trend, although is concerned regarding its safety [20]. ICSI is a more invasive procedure that associated with a higher time demands and costs and bypasses the natural mechanisms [21]. Analysis of three RCTs could not show any significant benefit of ICSI over IVF [22]. Thus, IVF can be considered as the second line of treatment, if no conception achieved after 3-4 cycles of IUI, no need for unnecessarily switching over to ICSI.

ICSI has completely changed the treatment of some forms of azoospermia. In obstructive azoospermia with surgical failure, spermatozoa may be recovered from either the testis or epididymis. In our study, ICSI has helped many couples with severe male factor infertility as in azoospermia and teratozoospermia to achieve pregnancies, so could be preserved to those mentioned abnormalities in which no pregnancy attained by either IVF or IUI although there is no statistically significant.

Previous literature [23] confirmed the adverse effects of smoking on the results of IVF and ICSI, in the present study the pregnancy rate was slightly lower among those who smoke but not reaching statistical significance. In the present study, there was no difference in the pregnancy outcomes between females with primary or secondary infertility by previous research [24]. Menogon associated with highest pregnancy rate 43.5% compared to other drug but no statistical significance. Inconsistent to the result stated by Lee C. et al. that Gonal-f resulted in a higher pregnancy rate [25].

The Study limitations were that: it was a retrospective study, it was conducted at a single centre so generalization cannot be assured. Furthermore, the cumulative success rate of different ART methods was not included in the paper.

Infertility is a subject of debate. Although there are considerable researches done on the infertile female, further larger, prospective, multicenter studies to address male factor infertility are highly needed.

In conclusion, there was no significant statistical difference in pregnancy outcomes regarding various assisted reproductive techniques, smoking, type of infertility and medications.

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References

1. Al-Turkey HA. Prevalence of primary and secondary infertility from a tertiary centre in eastern Saudi Arabia. Middle East Fertility Society Journal. 2015;20 (4): 237–240. https://doi.org/10.1016/j.mefs.2015.02.001

2. Haifa A. A 5-year analysis of semen parameters in Saudi Arabian men attending infertility clinics Journal of International Medical Research. 2016; 44(3): 656–661. https://doi.org/10.1177/0300060516632108 PMid:27036147

3. Agarwal A, Mulgund A, Hamada A, Chyatte MR. A unique view on male infertility around the globe. Reprod Biol Endocrinol. 2015; 13: 37. https://doi.org/10.1186/s12958-015-0032-1 PMid:25928197 PMCid:PMC4424520

4. Cooper TG, Noonan E, von Eckardstein S, Auger J, Baker HW, Behre HM, Haugen TB, Kruger T, Wang C, Mbizvo MT, Vogelsong KM. World Health Organization reference values for human semen characteristics. Hum Reprod Update. 2010;16(3):231-45. https://doi.org/10.1093/humupd/dmp048 PMid:19934213

5. Hughes EG, Collins JP, Garner PR. Homologous artificial insemination for oligo asthenospermia: a randomized controlled study comparing intracervical and intrauterine techniques. Fertil Steril. 1987;48(2):278-81. https://doi.org/10.1016/S0015-0282(16)59356-X

6. Ho PC, Poon IM, Chan SY, Wang C. Intrauterine insemination is not useful in oligo asthenospermia. Fertil Steril. 1989;51(4):682-4. https://doi.org/10.1016/S0015-0282(16)60621-0

7. Ombelet W, Bosnians E, Janssen M, Cox A, Vlasselaer J, Gyselaers W, et al. Semen parameters in a fertile versus subfertile population: a need for change in the interpretation of semen testing. Hum Reprod. 1997; 12: 987–993. https://doi.org/10.1093/humrep/12.5.987 PMid:9194652

8. Khorram O, Patrizio P, Wang C, Swerdloff R. Reproductive technologies for male infertility. J Clin Endocrinol Metab. 2001; 86(6):2373-9. https://doi.org/10.1210/jcem.86.6.7571 PMid:11397826

9. Palermo G, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single

spermatozoon into an oocyte. Lancet. 1992;340(8810):17-8. https://doi.org/10.1016/0140-6736(92)92425-F

10. Van Steirteghem AC, Liu J, Joris H, Nagy Z, Janssenswillen C, Tournaye H, Derde MP, Van Assche E, Devroey P. Higher success rate by intracytoplasmic sperm injection than by subzonal insemination. Report of the second series of 300 consecutive treatment cycles. Hum Reprod. 1993;8(7):1055-60. https://doi.org/10.1093/oxfordjournals.humrep.a138191 PMid:8408486

11. Shevell T, Malone FD, Vidaver J, Porter TF, Luthy DA, Comstock CH, Hankins GD, et al. Assistant reproductive technology and pregnancy outcome. Obstet Gynecol. 2005;106(5Pt 1):1039-45. https://doi.org/10.1097/01.AOG.0000183593.24583.7c PMid:16260523

12. Katzorke T, Kolodziej FB. The significance of insemination in the era of IVF and ICSI. Urologe A. 2010;49(7):842-6. https://doi.org/10.1007/s00120-009-2219-6 PMid:20238208

13. Hoffman B, Schorge J, Schaffer J, Halvorson L, Bradshaw K. Williams Gynecology. 2nd ed. New York: McGraw Hill, 2012:529-35.

14. Badawy A, Elnashar A, Eltotongy M. Effect of sperm morphology and number on success of intrauterine insemination. Fertil steril. 2009; 91(3):777-81. https://doi.org/10.1016/j.fertnstert.2007.12.010 PMid:18304534

15. Kastrop PM, Weima SM, Van Kooij RJ, Te Velde ER. Comparison between intracytoplasmic sperm injection and in-vitro fertilization (IVF) with high insemination concentration after total fertilization failure in a previous IVF attempt. Hum Reprod. 1999;14(1):65-9. https://doi.org/10.1093/humrep/14.1.65 PMid:10374096

16. Allen NC, Hebert M, CM, Maxson WS, Rogers BJ, Diamond MP, Wentz AC. Intrauterine insemination: a critical review. Fertil Steril. 1985;44(5):569-80. https://doi.org/10.1016/S0015-0282(16)48969-7

17. Zhao Y, Vlahos N, Wyncott D, Petrella C, Garcia J, Zacur H, et al. Impact of semen characteristics on the success of intrauterine insemination. J Assist Reprod Genet. 2004;21:143–8. https://doi.org/10.1023/B:JARG.0000031246.76666.f6 PMid:15279320 PMCid:PMC3455523

18. Cohlen BJ. Should we continue performing intrauterine inseminations in the year 2004? Gynecol Obstet Invest. 2004; 59: 3–13. https://doi.org/10.1159/000080492 PMid:15334020

19. Kossakowski J, Stephenson M, Smith H. Intrauterine insemination with husband's sperm: comparison of pregnancy rates in couples with cervical factor, male factor, immunological factor and idiopathic infertility.Aust N Z J Obstet Gynaecol. 1993;33(2):183–6. https://doi.org/10.1111/j.1479-828X.1993.tb02389.x PMid:8216122

20. Meschede D, Lemcke B, Exeler JR, De Geyter C, Behre HM, Nieschlag E, et al. Chromosome abnormalities in 447 couples undergoing intracytoplasmic sperm injection- prevalence, types, sex distribution and reproductive relevance. Hum Reprod. 1998;13(3):576-82. https://doi.org/10.1093/humrep/13.3.576 PMid:9572415

21. Staessen C, Camus M, Clasen K, De Vos A, Van Steirteghem A. Conventional in-vitro fertilization versus intracytoplasmic sperm injection in sibling oocytes from couples with tubal infertility and normozoospermic semen. Hum Reprod. 1999;14 (10): 2474-2479. https://doi.org/10.1093/humrep/14.10.2474 PMid:10527972

22. Tournaye H, Verheyen G, Albano C, Camus M, van Landuyt L et al. Intracytoplasmic sperm injection versus in vitro fertilization: a randomized controlled trial and a metaanalysis of the literature. Fertil Steril. 2002; 78: 1030–7. https://doi.org/10.1016/S0015-0282(02)03377-0

23. Boulet SL, Mehta A, Kissin DM, Warner L, Kawwass JF, Jamieson DJ. Trends in use of and reproductive outcomes associated with intracytoplasmic sperm injection. JAMA. 2015;313(3):255-63. https://doi.org/10.1001/jama.2014.17985 PMid:25602996 PMCid:PMC4343214

24. Kovac JR, Khanna A, Lipshultz LI. The effects of cigarette smoking on male fertility. Postgrad Med. 2015;127(3):338-41. https://doi.org/10.1080/00325481.2015.1015928 PMid:25697426 PMCid:PMC4639396

25. Lee C, Keith J. A Retrospective Review Comparing the Use of Gonal-Fand Metrodin-HP for In-Vitro Fertilisation (IVF). Med J Malaysia. 2003;58(1):95.