

Demographic determinants and outcome of in vitro fertilization (IVF) services in Saudi Arabia

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Abstract

Objectives: To assess the demographic characteristics and outcomes of couples undergoing in vitro fertilisation (IVF) treatment at a private hospital in Al Qassim district, Saudi Arabia.

Methods: For this retrospective study, information was extracted from the hospital electronic database and IVF unit medical records.

Results: 2259 couples underwent 2703 IVF/ICSI cycles during 2014 to 2016. The utilization rate was approximately 1000 cycle per million of inhabitants. Mean ages \pm standard deviation (SD) for women and men were 32.9 ± 5.7 and 39.2 ± 7.4 years, respectively. More couples were diagnosed with secondary infertility (55.2%) than primary infertility (44.8%). Male factor was the commonest single indication for IVF (36.2%). Mean \pm SD infertility duration was 4.70 ± 4.03 years. Overall, 949 couples had a successful pregnancy. Age-specific pregnancy rates (PR) were highest for women <35 years (39.8%) and lowest for women >40 years (11.6%). Male age and infertility duration had no effect on PR but sperm source (fresh vs. frozen) and female age had significant impacts. However, fresh sperm was used in 90.6% cycles whereas frozen sperm was used in 9.4% cycles.

Conclusions: IVF treatment outcomes in the Al Qassim district are within the boundaries of average international success rates. Infertile couples seeking IVF services should be counselled with regard to important prognostic factors

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Keywords

IVF/ICSI outcome, infertility, assisted reproductive technology, Saudi Arabia

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Introduction

Parenthood is one of the most universally desired goals for couples. However, not all couples will achieve spontaneous pregnancy and a proportion may need medical help to resolve underlying fertility problems. Infertility has been recognized as a public health issue worldwide by the World Health Organization (WHO).¹ Management options available to infertile couples consist of three main interventions; medical, surgical and assisted reproductive technology (ART). ART allows clinicians and scientists to perform fertilization and early embryonic growth outside the human body. Therefore, the procedure bypasses several pathological conditions in women, including fallopian tube blockage and ovarian factors, and in men circumvents obstructive azoospermia and other sperm dysfunctions which are not curable by other medical or surgical options.² The choice of treatment depends on the cause, efficacy, cost, and availability of options and may be affected by cultural and religious considerations.^{3,4}

The first successful birth following an *in vitro* fertilization (IVF) procedure was in 1978.⁵ Since then, IVF and other techniques such as intracytoplasmic sperm injection (ICSI) have been implemented in clinics around the world to assist infertile couples. Indeed, it was estimated that from its inception in 1978 to 2012, approximately 6.5 million babies have been born worldwide by ART with vast differences in availability, practice and results.⁶

IVF services in the Middle East were initiated in the mid 1980's and were started in

the Kingdom of Saudi Arabia (KSA) in 1986. The service is practiced in a strictly religious manner and certain aspects of the technology such as sperm and oocyte donation are prohibited.⁷ Currently, there are more than 35 ART centres performing around 20,000 IVF treatment cycles per year in the KSA and most of them are in the private sector. Although several medical professionals working in Saudi ART centres have published their experiences,⁸⁻¹⁰ there is no national registry for ART in the KSA. In addition, there has been little participation from Saudi ART clinics in regional registries such as the Middle East Fertility Society (MEFS) or global registries such as the International Committee Monitoring Assisted Reproductive Technologies (ICMART).¹¹

The aim of this present study was to assess the demographic characteristics of couples seeking IVF treatment in a private hospital in Buraydah, Al Qassim district, KSA and evaluate the ART outcomes.

Methods

Couples undergoing IVF procedures at Dr. Sulaiman Al Habib Al Qassim Hospital, Buraydah, Al Qassim district from January 2014 to December 2016, were included in this study. Patient data was extracted from the hospital electronic database and IVF unit medical records. Patients who had cryopreserved IVF cycles, cancelled cycles or were lost-to-follow up for pregnancy and IVF outcome were excluded from the study. Demographic data were

obtained and included ages of the couple, infertility duration, reason for IVF treatment, type and cause of infertility and source of sperm. Clinical pregnancy had been confirmed by visualization of foetal cardiac activity on ultrasound on day 35 following embryo transfer.

All clinical and laboratory protocols were approved by the Institutional Review Board and Ethics Committee of Dr. Sulaiman Al Habib Medical Group- Al Qassim Hospital. This was a retrospective analysis of data and so written informed consent from participants was not required.

Statistical analyses

Statistical analyses were performed using SPSS software (version 21.0 for Windows®; (IBM SPSS, Armonk, NY: IBM Corp, USA). Student's t-test was used for numerical variables, χ^2 tests for categorical variables and multivariate logistic regression analysis was used to examine the impact of various factors on the pregnancy rate (PR). Two-tailed tests were employed and $P < 0.05$ was considered to indicate statistical significance.

Results

In total, 2259 couples underwent 2703 IVF/ICSI cycles during the study period. The total number of IVF cycles reaching oocyte aspiration stage was 2947 but 244 cycles were not completed and excluded from the analyses. Demographic characteristics for all couples are shown in Table 1. For women, mean age \pm standard deviation (SD) was 32.9 ± 5.7 years and ranged from 16 to 48 years. For men, mean age \pm SD was 39.2 ± 7.4 years and ranged from 22 to 83 years. Distribution of ages is shown in Table 2. Most women were under 38 years of age whereas most men were older than 38 years. In approximately 58% of couples, the woman was younger than

Table 1 Demographic characteristics of the participants

Characteristics	
Total number of couples	2259
Total number of cycles	2703
Female age, years	32.9 ± 5.7
Male age, years	39.2 ± 7.4
Duration of infertility, years	4.70 ± 4.03
Primary infertility	1012 (44.8)
Secondary infertility	1247 (55.2)
Total number of couples with a successful pregnancy	949
Overall pregnancy rate*	(35.1)
Number of IVF cycles	1.5 ± 0.95

Values are shown as *n*, *n* (%) or mean \pm SD.

*The number of clinical pregnancies diagnosed by ultrasonography or clinical documentation per 100 embryo transfer procedure¹¹.

Table 2 Age groups of couples

Age Group years	Women	Men
<35	1565 (57.9)	609 (22.5)
35–37	512 (18.9)	315 (11.7)
38–40	393 (14.5)	1070 (39.6)
>40	233 (8.6)	709 (26.2)

Values are shown as *n* (%).

35 years and only 8.6% of women compared to 26.2% of men were >40 years.

Secondary infertility was slightly more common than primary infertility (55.2% vs. 44.8%) (Table 1). Interestingly, 4.9% of women had been previously married, 23.1% were multipara, 44.0% had at least one previous living child and two already had 10 children. Most cases were in a first treatment IVF cycle (67.1%). However, 21.1% cases were in a 2nd cycle, 11.3% in a 3rd–5th cycle and <1% had >5 IVF cycles. For 52.4% of cases, previous ART treatment at other IVF units had been obtained. Male factors accounted for 36.2% of the indications for ART procedures followed

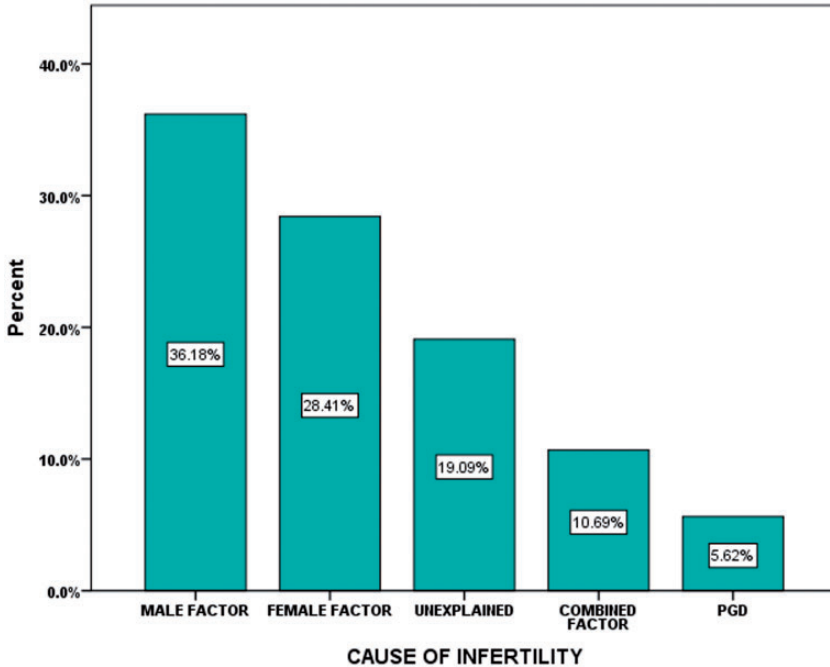


Figure 1 Indications for assisted reproductive technology (ART)

y axis =percentage of couples

PGD, preimplantation genetic diagnosis

by female factors (28.4%), unknown factors (19.1%) and combined factors (10.7%) (Figure 1). For 5.6% of couples, the reason for IVF treatment was preimplantation genetic diagnosis (PGD). Mean infertility duration \pm SD was 4.70 ± 4.03 years and ranged from 1 to 25 years. Long standing infertility of ≥ 5 years was recorded for 42.4% of cases. Infertility duration groups and successful pregnancy rates for all cycles are shown in Table 3.

Fresh ejaculated sperm was used in 2448 cycles (90.6%), whereas frozen testicular sperm was used in 255 ICSI cycle (9.4%). Overall, 949 couples had a successful pregnancy. The overall clinical PR per embryo transfer, defined as the number of clinical pregnancies diagnosed by ultrasonography or clinical documentation per 100 embryo transfer procedure,¹¹ was

35.1% (949/2703). However, PR for the fertile couples who undertook PGD was 50%. Sub-group analysis across different age groups showed that PR declined as female age increased (Table 4). Highest PR rates were found in women < 35 years (39.6%), followed by women 35–37 years age (35.7%) and women 38–40 years age (29.5%). Only 11.6% of women > 40 years became pregnant. For men, PR was also highest in those aged < 35 years (40.4%) and lowest in those > 40 years (26.9%) but for men aged 38–40 years the rate was 37.8% (Table 5). There was no statistically significant difference in PR between couples with primary and secondary infertility (35.4 versus 36.1%, respectively). The overall PR per aspiration (i.e., cycles with successful pregnancy/cycles reaching oocyte aspiration stage was 32.2% (949/2947).

Table 3 Infertility duration groups and successful pregnancy rates for all cycles

Duration years	Number of cycles n (%)	Successful pregnancy n	Pregnancy rate* %
1–4	1561 (57.8)	568	36.4
5–9	799 (29.6)	277	34.7
10–14	263 (9.7)	86	32.7
15–25	80 (3.0)	18	22.5
Total	2703	949	35.1

*The number of clinical pregnancies diagnosed by ultrasonography or clinical documentation per 100 embryo transfer procedure¹¹

Table 4 Female age groups and successful pregnancy rates

Age Group years	Successful pregnancy n	Pregnancy rate* %
<35	623	39.8
35–37	183	35.7
38–40	116	29.5
>40	27	11.6

*The number of clinical pregnancies diagnosed by ultrasonography or clinical documentation per 100 embryo transfer procedure¹¹

Table 5 Male age groups and successful pregnancy rates.

Age Group	Successful pregnancy n	Pregnancy rate* %
<35	246	40.4
35-37	108	34.3
38-40	404	37.8
>40	191	26.9

*The number of clinical pregnancies diagnosed by ultrasonography or clinical documentation per 100 embryo transfer procedure¹¹

Logistic regression analysis showed that male age and infertility duration did not affect PR (Table 6). However, female age and sperm source had significant impacts

Table 6 Regression analysis showing the impact of sperm source, age of couple and infertility duration on pregnancy rates.

	Odds ratio	95% CI	Statistical Significance
Sperm source*	1.50	1.1, 2.1	$P = 0.019$
Female age	1.04	1.01, 1.1	$P < 0.001$
Male age	0.99	0.97, 1.0	<i>ns</i>
Infertility duration	0.98	0.96, 1.0	<i>ns</i>

*Fresh or frozen.
ns, not significant.

on PR. Sub-group analysis of female age groups showed that <35 years and 35–37 years had more positive impacts on PR (OR: 16.5 [95% CI 2.2,122]; $P < 0.001$ and OR:13.1 [95% CI 1.8, 97.3]; $P < 0.001$, respectively) than patients >40 years. Fresh sperm had been used in 90.6% cycles whereas frozen sperm was only used in 9.4% cycles and this may have influenced the results.

Discussion

This retrospective study was designed to assess demographic and outcome data from couples seeking IVF treatment in a private hospital in the Al Qassim district, Saudi Arabia. The average age of the couples involved in this study was similar to that from two other previous studies in government facilities in KSA.^{12,13} One of the previous studies collected data from infertile couples attending an IVF clinic in Riyadh,¹² and the other from an infertility clinic without IVF facilities in Al-Khobar, Eastern KSA.

For this population, secondary infertility rates were higher (55.2%) than primary infertility rates (44.8%). These data are consistent with results of a retrospective analysis of 70 patients attending a gynaecological clinic at the Riyadh Military Hospital,¹⁴ but are dissimilar to data from a hospital in Al-Khobar where there were

more cases of primary infertility than secondary infertility (80.5% vs.19.5%).¹³ The discrepancy in findings may be attributed to differences in awareness of ART and availability of IVF services in different regions of KSA. For example, in the Al-Khobar region in Eastern Saudi there are only four, private, IVF centres serving >4.1 million people. By contrast, in the Al Qassim District there is one private hospital and one government unit providing IVF services to approximately 1.4 million people. This explanation is supported by our observation that 52.4% of the couples in this present study had history of previous IVF treatment.

Although the average duration of infertility for this sample was approximately five years, 42.4% of cases had long standing infertility of ≥ 5 years. These data suggest that for nearly half the couples there was a delay in seeking medical assistance. A possible explanation for this reticence may be the relatively high costs of fertility treatment which are not covered by medical insurance and may be prohibitive for many couples.

The European Society of Human Reproduction and Embryology (ESHRE) estimated that across all countries there is an annual requirement of ART services of 1500 cycle per million of population,¹⁵ but there are marked international differences in the availability and uptake of ART treatments. For example, in the USA the utilization rate is low at 373 cycles per million per annum, whereas in Australian and Scandinavian rates are 1574 and 1465 per million per annum, respectively.¹⁶ In 2002, the uptake of ART services in Saudi Arabia was estimated to be 242 cycles per million per annum.¹⁷ However, current estimates from the Al Qassim District (i.e., 1100 cycle per annum from a private hospital and 600–800 cycles/per annum from a government unit, covering a population of approximately 1.4 million people) suggest

that the utilization rate is approximately 969 cycles per million per annum in this region. These data suggest that there has been a significant increase in uptake of ART services in KSA over recent years and that current rates are now comparable with estimated European rates of 1252 cycles per million per annum.⁶

The reasons provided for IVF treatment in this study were similar to those in a previous Saudi study and male, female and unknown causes were the most common factors for infertile couples.¹² Interestingly, approximately 6% of the couples had used IVF treatment for PGD. Indications for PGD in fertile couples include medical and social reasons. In addition, parents with children needing hematopoietic stem cell transplants have used PGD to assure that a child is a human leukocyte antigen (HLA) match with an existing child.¹⁸

The overall PRs per aspiration and per embryo transfer were 32.2% and 35.1%, respectively, which are slightly higher than the rates of 29.6% and 32.3% reported in a European IVF-monitoring study.⁶ By comparison, the latest ICMART report which covers 2008–2010, reported PR per aspiration for fresh IVF/ICSI cycles of 42.0%, 33.6%, 29.6%, and 27.8% for North America, Middle East (Egypt and Lebanon), Europe, and globally, respectively.¹⁹ The high PR reported in North America and Middle East may be attributed to the high number of embryos transferred; ≥ 4 embryos were transferred in 13.5% and 18.7% of cycles in North America and Middle East, respectively.¹⁹ Our unit has a strict policy of transferring no more than three embryos in any fresh or frozen cycle.

Although, women were younger than men in 58% of the couples, logistic regression analysis showed that female age had a significant impact on PR and younger age groups had a greater influence than older age groups. These findings are consistent

with previous IVF studies that have shown advanced maternal age was significantly associated with reduced PR.^{20–22} Interestingly, studies examining the effects on PR of the indication for IVF and the duration and type of infertility have shown inconsistent results.^{21–23} In this present study, sperm source also had a significant effect on PR but fresh sperm had been used in 90.6% cycles compared with frozen sperm which was only used in 9.4% cycles and this imbalance may have affected the results.

Limitations of the study include a possible bias because only one centre was involved. Nevertheless, the sample size was large and the centre is the largest service provider of IVF in the KSA. Dr. Sulaiman Alhabib Medical Group is the largest service provider in KSA ; it own 4 units 3 in Riyadh and 1 in Qassim where this study was conducted. In addition, the retrospective nature of the analysis with irretrievable information for some patients may have also affected the results. Indeed, several categories of sociodemographic data, such as residency area, educational and income levels and smoking history were missing and may have provided a more complete description of the study population.

In conclusion, our retrospective study found that IVF treatment success rate in the Al Qassim District, Saudi Arabia was within the boundaries of average international success rates.^{5,14} The utilization rate was approximately 1000 cycle per million of inhabitants. Secondary infertility was more common than primary infertility and male factors were the most common cause of infertility. Of all the factors that were examined for an effect on PR, female age had a clear impact.

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Declaration of conflicting interests

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