The Relationship between Seasonal Variability and Pregnancy Rates in Women Undergoing Assisted Reproductive Technique

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Backgrownd: Studies in regions with seasonal climatic variations have revealed a correlation between human natural conception and birth rates. Holidays and other cultural activities probably have influence on conception, but the ambient temperature and emotional influences on the female hormones related to fertility may play an important part in the seasonal variation in conception.
Objectives: The aim of study was to determine the relationship between the success rate of Assisted Reproductive Technique (ART) treatment cycles and temperature in different seasons.
Materials and Methods: A retrospective study on all individuals undergoing assisted ART at our institution was performed during June 2000 to June 2001. The study population represented 258 IVF-ET cycles and 821 ICSI treatment cycles. Different variables were analyzed using χ^2 test.
Results: In IVF treatment cycles, conception was more common from early spring (March to June). This decreased from spring, with the minimum in fall, 22% and 14%, respectably. A significant seasonal variability in the number of eggs, embryo transferred and sperm motility was not demonstrated (p>0.05), but sperm count was significantly higher in spring than any other season ($72\pm4 \times 10^6$ and $52\pm7 \times 10^6$, respectively).
Conclusion: The seasonal changes should be taken into account together with other factors when evaluating infertility data.

Keywords: Seasonal variation, Pregnancy rate, IVF-ET, ART, Infertility

Introduction

Fifteen percent of couples do not achieve pregnancy after one year of unprotected sexual intercourse (Tuerlings 2000) and at the end of their reproductive life, 2-7% of couples remain childless. Assisted Reproductive Techniques (ART) have become an established treatment for certain types of human infertility, with a high fertilization rate (Edirisinghe *et al.*, 1997).

ARTs used for fertilization of human oocytes in vitro are extremely effective and the overall fertilization rates are now consistently about 60-80% in programs per inseminated eggs IVF treatment cycle (Bedford and Kim 1993). But the success rate is dependent on several factors such as cause of infertility, kind of treatment, ovulation induction methods, drugs, and environment factors

as well (Gavrilov and Gavrilova 1999; Lerchl *et al.*, 1993). Natural environmental factors have also been shown to play a critical role, notably in terms of synchronizing built-in rhythms (Halberg *et al.*, 2000; Halberg *et al.*, 2001). Of these, temperatures and seasons have been suggested as environmental factors that influence fecundity in mammals. It has been reported that there is a link between human fertility, temperature and seasonal birth patterns. Seiver (1985) found that in the past few decades, the American states that had the largest decline in the April-May trough in births were also those that saw the highest increases in air conditioning. Furthermore, it has been reported relatively large seasonal fluctuations among lower-income groups in the United States (White and Hertz-Picciotto 1985).

The correlations between weather and fertility have been stablished from data from England. It estimated the effects of temperature on births seven to eleven months later. Extreme weather was found to lead to a decline in births—"The negative effects of cold and heat on births 10 and

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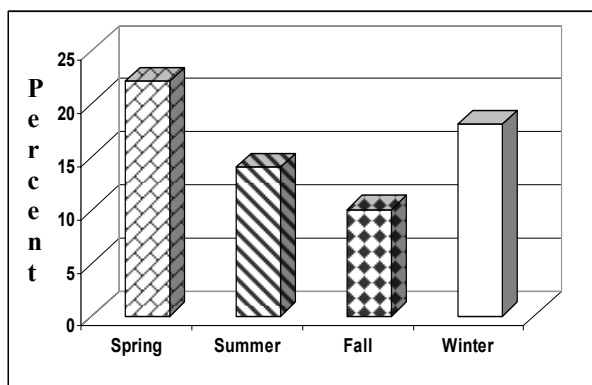**E-mail:** kalantarsm@ystp.ac.ir

Figure1. Pregnancy rate following IVF treatment cycles in different seasons.
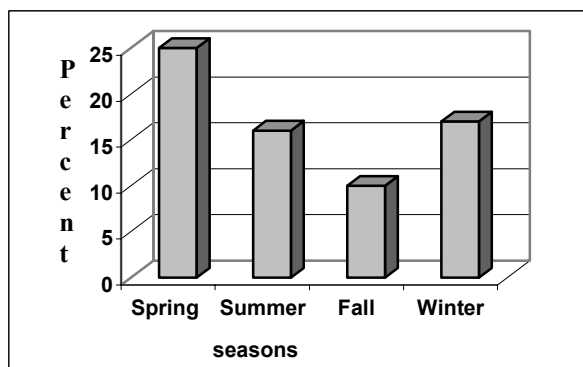

Figure2. Pregnancy rate following ICSI treatment cycles in different seasons

11 months later is attributed to effects working through morbidity, which may have caused delayed effects on fecund ability and intrauterine morality" (Miron, 1996).

The aim of the study was to examine biological factors in seasonal variation to determine the relationship between the success rate of ART treatment cycles and temperature in different seasons.

Materials and Methods

A retrospective study on all individuals undergoing assisted reproductive technique (ART) at our institution was performed during June 2000 to June 2001. Totally, 1147 ART treatment cycles from 951 infertile couples were reviewed. The study population represented 258 IVF-ET cycles and 821 ICSI treatment cycles that were performed consecutively at the Yazd Research & Clinical Center for Infertility and Madar Hospital for Women. The patients excluded from the analysis were those who had undergone treatment cycles without embryo transferred (n=68 cycles). The induction procedure was done as previously described (1,9). Oocytes were aspirated
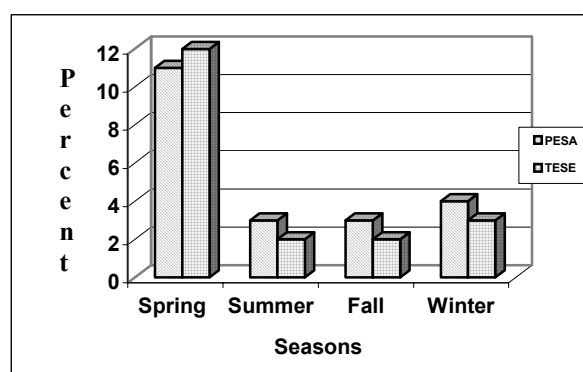

Figure3. Pregnancy rate from sperm obtained by PESA or TESE and ICSI treatment cycles in different seasons

transvaginally with ultrasound guidance 35 hours after the CG administration. Oocytes were cultured in Ham's F10 medium supplemented with 10% HAS. Insemination was carried out 4-6 hours following oocyte recovery using 50,000-100,000 motile spermatozoa/ml, which were separated from seminal plasma by Percoll preparation. On day 1, 18-20 hours after insemination (IVF), fertilization was confirmed when two pronuclei (normal IVF) or more pronuclei (poly pronucleus FR) were present. All embryos were graded on respect ion 1-4 scales and then the best quality were selected and replaced in the female uterus. A quantitative serum HCG assay was drawn on the fourteenth day after ET. Values of <5mIL/mL were considered negative. Patients who had a positive testing were then monitored by a sonogram during the fourth week after transfer to establish viability.

A questionnaire providing information on treatment cycles such as female's age, number of retrieved eggs, embryo transferred and result of semen analysis was completed for each cycle.
The cycles were classified according to the season when the treatment was performed. The χ^2 test was used for the comparison of the results of different variables between each group. $P<0.05$ was considered statistically significant.

Results

In this study, we retrospectively compared the percentages of number of eggs retrieved, embryos, number of embryo transferred (ET), pregnancy rate (βHCG), and sperm characteristic such as sperm morphology, sperm motility and sperm count relative to the season variation from a total of 1079 treatment cycles. The pregnancy rate was significantly higher in spring (11/50 IVF cycles and 39/195 ICSI cycles) than other seasons (p<0.05), either by IVF treatment cycles (Fig.1) or by ICSI treatment cycles (Fig.2). It interestingly

Table I. Characteristic of IVF treatment relation to the season variation.

Variables		Spring	Summer	Fall	Winter
Women's age		33±4	31±3	31±4	32±4
No. of egg retrieved		7±3	8±2	6.5±3	7±1
No. embryo transferred	3.1±1	2.9±0.4	3.3±0.8	3.0±1	
Sperm count $(\times10^6/ml)$*	72±14	52±17	58±14.5	65±9	
Sperm motility (%)		61±7	65±4	58±6	55±3

Sperm motility includes motility grade I+II according to the WHO, criteria 1998.
*$P<0.05$ was assigned significantly difference.

Table II. Characteristic of ICSI treatment relation to the season variation.

Variables		Spring	Summer	Fall	Winter
Women's age		30±4	32±3	29±5	30±3
No. of egg retrieved		11±4	9±3	6±4*	10±3
No. embryo transferred	3.1±0.9	3±1	2.1±0.6	2.8±1	
Sperm count $(\times10^6/ml)$*	8±2	12±4	9±3	11.5±3.7	
Sperm motility (%)*	12±5.5	18±4	22±9	14±6.4	

Sperm motility includes motility grade I+II according to the WHO, criteria 1998.
* $P<0.05$ was assigned significantly difference.

dropped to 14% (11/79, IVF cycles) and 14% (27/194) during fall. With regard to the different variables in IVF treatment cycles, only sperm count was significantly different. Sperm count in the spring (72±14 x 10^6/ml) was higher than the summer (52±17 x 10^6/ml, Table.I). In the case of ICSI treatment, cycles sperm motility and concentration were significantly different between the season. Sperm concentration was higher in summer (12±4) while sperm motility was higher during fall (22±9, Table II). Also, the number of retrieved eggs was significantly lower in fall than the other seasons (6±4, Table.2). As it has shown in Fig.3, pregnancy rate from sperms obtained by PESA or TESE after ICSI treatment cycles in different seasons was compared again; in spring time, the percentage was higher (10.2% and 11.5%, respectively) than in other seasons. But there was a similar result between those kinds of sperm source in different seasons time (Fig.3).

Discussion

Annual birth rates have been found to be affected up to 10-20% by seasonal variation. Variations affecting birth patterns are attributed to biological and social factors: annual rhythms of climatic conditions, or the photoperiod and varying sexual activity (Lerchl et al., 1993).

Instead of using data on conceptions, births have been included as the variable to be explained. Natural environmental factors have been shown to play a critical role, notably in terms of synchronizing built-in rhythms (Halberg et al.,

2001). Our study revealed that the pregnancy rate in ART is closely related to the seasons, where the pregnancy rate is higher during spring than at any other time. These findings corroborate the hypothesis that fecundity in mammals and human is dependent on daylight and temperature during different seasons as previously reported (Heideman 2004; Peltoniemi et al., 2000; Place et al., 2004; Weber et al., 1998).Epidemiological studies suggest that the inhibition of fertility in men in summer contributes to the seasonal variation in human reproduction in the lower latitudes and also that stimulation of fertility by lengthening of the photoperiod in spring contributes to the variation at higher latitudes. Parallels between the seasonality of human reproduction and seasonal affective disorder suggest that they may be governed by common biological processes (Wehr 2001). It has been proposed that human fertility has a link with temperature and seasonal birth patterns. Seiver (1985) found that in the past few decades, the American states that had the largest decline in the April-May trough in births were also those that saw the highest increase in air conditioning. Acorrelation between weather and fertility was found using monthly data for England. It estimated the effects of temperature on births seven to eleven months later (White and Hertz-Picciotto 1985). Extreme weather was found to lead to a decline in births. Lam and Miron (1996) studied the effects of temperature on human fertility. They used monthly birth and temperature data for 46 years, from 1942, to study the effect that temperature had on seasonal variations in births for the different states in the U.S. Their results show that

temperature has quantitatively important effects on both seasonal and non-seasonal variation in births. Therefore, temperature only explains a portion of the seasonal variation in birth patterns (by affecting coital frequency). A number of physiological facts also help explain the seasonality. For example, a hormonal production called photoperiod, that regulates fertility, is affected by the length of day. Heat has also been found to have negative effects on sperm count and sperm quality. Sperm quality is lowest in July through September (the hottest months in the U.S.) and highest in February and March. There were significant differences between success rates for procedures carried out in the months with the most daylight hours - May to September - compared to those with the least - November to February, in 3,000 IVF cycles carried out between 1997 and 2001 (Wood *et al.*, 2004). They concluded that patients might have a better chance of a successful pregnancy in summer.

Rojansky and colleagues (2000) reported that, during the spring, the highest fertilization and quality of embryo were observed and, in the autumn, the lowest. These changes correlated with the absolute number of light hours and its increment over time, but not with the temperature, humidity, or other environmental parameters. While Paraskevaide *et al.*, (1998) conception was more common from early winter until early spring (Oct. to March) with a peak in Nov, using donor sperm. Our results revealed that highest sperm count was in spring. At this time, the temperature in Yazd is usually $32\pm5\ ^0C$.

There are several explanations for seasonal variation and fertility rate. Local effects of a hormone called melatonin may therefore be responsible. Melatonin levels naturally cycle in response to light and dark, and all mammals have physical responses to this cycle, the most obvious being the natural sleep/wake patterns. Until recently it was thought that melatonin acted only through the pituitary gland in the brain. It's secreted by the pineal gland, a pea-size structure at the center of the brain, as our eyes register the fall of darkness." At night, melatonin is produced to help our bodies regulate our sleep-wake cycles (Lam *et al.*, 1994; Place *et al.*, 2004). Wood *et al.*, 2004 reported that fewer drugs were significantly required to stimulate ovulation in women during the months with most daylight.

Nevertheless, there are several factors might be influence on gametes function and/or hormonal profile of human conception and mammals as well. This study was not concerned with such abnormalities such as endometriosis, or the female's hormonal profile which may be decrease implantation and pregnancy rate.

These results indicate an effect of seasons on in-vitro production but more data are needed to conclude the exact time for best results.

Acknowledgments

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