Research Article

Gynecology & Reproductive Health

Season Variability in Pregnancy and Live Birth Rates for Women Undergoing Assisted Reproductive Technique: A Retrospective Study

Samar Abdelwehab[1*], Basma Abdelnasser[2] and Mahmoud Samy[3]

[1]*Clinical Embryologist ESHRE Certified, Egypt.*

[2]*Andrologist, Egypt.*

[3]*Consultant Obstetrics and Gynecology, MRCOG, MFFP.*

[*]Correspondence:
Samar Abdelwehab, Clinical Embryologist ESHRE certified, Egypt, E-mail: s.abdelwehab@hotmail.com.

Received: 17 December 2017; **Accepted:** 04 January 2018

Citation: Samar Abdelwehab, Basma Abdelnasser, Mahmoud Samy. Season Variability in Pregnancy and Live Birth Rates for Women Undergoing Assisted Reproductive Technique: A Retrospective Study. Gynecol Reprod Health. 2018; 2(1): 1-4.

ABSTRACT

Objectives: *Investigation for seasonal variability in pregnancy and live birth rates among women undergoing Assisted Reproductive Techniques (ART).*

Design: *We did a retrospectives study of the pregnancy, implantation and live birth rates of the women who did ART in our centre over the past three years, 2014-2016. During that time 1451 patients had ICSI cycles. We selected 1219 patients from these for the purpose of this study.*

Patient selection criteria were women under 35 years of age and where ejaculated semen was used over a count of 1,000,000/ml or more. We analysed pregnancy, miscarriage and live birth rates according to the seasons patients had their cycle to accurately try to pinpoint if there was a favorable time of the year that increased pregnancy rates.

Results: *There was no significance difference in pregnancy, miscarriage and live birth rates between the four seasons.*

Conclusions: *Seasonality does not seem to affect pregnancy and live birth rates. It should not be taken into account for patients seeking ART.*

Keywords
Women, Birth rate, Pregnancy, Sperm cell count, IVF.

Introduction
We all know that there is seasonal variability in mammalian animals. The terms ‘spring lamb’ and ‘spring chicken’ refers to times when these animals were born during spring. There have been quite a number of articles investigating if there is seasonal variability in human pregnancy and birth rates during the year.

Levitas et al. [1] had a study showing seasonal variation of sperm cell count, motility and morphology, which showed better motility and morphology in winter months. This can be explained by the cool weather favoring sperm production.

There have also been a number of papers published studying seasonal variations in pregnancy and birth rates. An interesting paper done by William H. James [2] shows that there is seasonal variation in pregnancy and birth rates between different continents. In his study it was shown that the seasonal pattern of births in Europe showed an increase in spring and a decrease autumn. In contrast, the pattern in the US was of an increase in spring and a decrease in autumn.

He concluded that “The magnitude of seasonality correlates positively with latitude: it is suggested that this is partially consequent on variation in luminosity”. Perhaps there is an optimum window of temperature and humidity for the lab in each country that increases this natural variation if there is one at all.

According to Martinez Bakker et al. [3] who carried out a retrospective study across America for 78 years, she concluded the peak or optimum season for birth was affected by region and latitude. It would be interesting to see of a similar pattern occurred in IVF centres as well.

A similar study carried out by Rojansky et al. [4] shows seasonal variation in ART pregnancy outcomes. Other studies [5-8] also showed some seasonal variability in ART cycles. However some studies [9-11] showed no significant changes in pregnancy rates in their IVF centres. We wanted to carry out a similar study in our laboratory to find out if there was indeed some variation. If variation was directly related to temperature and humidity in our laboratory or simple seasonal variation due to the changing light/dark cycles that occur with the seasons?

An interesting study showing ova maturation rates in relation to the seasons [12,13] showed a peak of ova maturation during breeding seasons of the squirrel [12] and rhesus monkeys [13].

During this IVF study using non-human primates, the monkeys were kept in constant light/dark, temperature and food conditions yet these seasonal changes persisted. If humans are have similar endogenous chronobiological rhythm it may explain why there might be a seasonal pattern or peaks of fertility.

Assisted Reproduction is a good tool to use to assess this, as most factors are tightly controlled and monitored in the laboratory. We have retrospectively collected data from patients in our centre during the past four years starting January 2014- December 2016, to find out if there is indeed a seasonal variability in ART.

Materials and Methods

The Al-Samy Fertility Centre is located in Mansoura, in the North Delta region of Egypt. It serves Mansoura city and other neighboring towns and villages. It has a turnover of approximately 480 cycles a year. The andrologist and myself collected the data from the units' charts spanning the three-year period used in this study.

Patients

We retrospectively analysed 1451 cases spanning the three-year period of 2014-2016. The mean age was 28.42+- 4.86 and the overall pregnancy rate was 48.9% per embryo transfer. Live birth rate was 70.4%. Since gamete donation is prohibited in the country all couples used their own gametes.

To avoid many factors skewing the integrity of the study we only included patients less than 35 years and excluded couples that were using surgically extracted sperm for the ICSI cycle. As is the norm in our country. Intracytoplasmic Sperm Injection (ICSI) was done to all the couples seeking treatment in our centre. We also excluded cases were no fertilisation occurred thus we analysed 1219 cycles.

Complete infertility investigations of both partners (hormonal, gynecological ultrasound, hysterosalpingography (HSG) and semen analysis) were done before each couple embarked treatment. An agonist protocol using rFSH for ovarian stimulation was used. Oocyte retrieval was done 36.5 +- 1 hour after hCG administration.

We analysed pregnancy, miscarriage and live birth rates by month to see if there was any particular peak in any particular season throughout the years. We done divided the year into four seasons, three months each as follows;
Winter: December-February
Spring: March-May
Summer: June-August
Autumn: September-November

This seasonal division was made according to the weather in Egypt. The mean age (+-SD) was 28.42+- 4.86 (range 16-45). The patients were included in the month on which day of collection was done.

Statistical Analysis

Data was entered and statistically analysed using the Statistical Package for Social Science (SPSS) version 20. Qualitative data were described as numbers and percentages. X2 test and Monte Carlo test were used for comparison between groups as was appropriate. Quantitative data was described as means Standard Deviation (SD) or medians, as appropriate. They were tested for normality by Kolomogorov-Smirnov test. 'p value <_0.05' was considered to be statistically significant.

Results

We calculated the pregnancy rates of the selected women per month for the past three years and per season to see if there was any statistical significance. We divided the year into four seasons. Winter, Spring, Summer and Autumn. The results are as illustrated in the following charts.

	Winter	Spring	Summer	Autumn	P value
Age	28.4 ± 4.7	28.8 ± 5.1	28.6 ± 4.8	27.8 ± 4.8	0.054
Clinical Pregnancy	152/319 (47.6%)	150/271 (55.4%)	145/328 (44.2%)	149/301 (49.5%)	0.48
Miscarriage	18/139 (12.4%)	11/124 (8.9%)	17/136 (12.5%)	20/128 (15.6)	0.43
Live Birth Rate of Pregnant women	99/139 (71.2%)	87/124 (70.2%)	94/136 (69.1%)	91/128 (71.1%)	0.9

Table 1: Showing results of the seasons throughout period of study.

Discussion

Reading articles published on this topic there was a wide discrepancy between results of various studies. In this study we found no statistical difference between the seasons during all three years.

However some aspects of similar studies were quite intriguing. For example in Rojanski's 2000 study4 he found the best embryo and fertilisation rates were in spring. Despite this the worst pregnancy rates were also in spring. On the other hand the worst fertilisation and embryo quality rates were in autumn, but this season had the best pregnancy rates.

Are there some other unknown factors apart from embryo quality that can predict pregnancy? It certainly is food for thought. However it is also not fair to compare these studies, as there are quite a number of differences between them. Some studies include patients in the month in which they started ovarian stimulation, others the day of egg collection, which can cause a shift of two weeks or more. There is also a wide difference of inclusion criterion and what stimulation protocols were used.

Our results showed no significant differences in pregnancy or implantation rates between the seasons. Our results concur with other studies also showing no differences in the results of ART done in different seasons [7,10,11].

One reason why there might be a lack of seasonal variation in patients undergoing ART treatment is the fact that they are receiving treatment. If seasonal variation is indeed present in sperm count and motility1 then this is irrelevant as in an ICSI cycle we select a few top morphologically motile sperm to inject a specific number of eggs.

Our results also show no significant seasonal differences in the miscarriage and live birth rate, pointing to an absence of a seasonal change in endometrial receptivity. This could be explained by the hormonal suppression of the hypothalamic pituitary axis and exogenous administration of gonadotropins for ovulation stimulation in an ICSI cycle.

Two studies Wunder [9] and Weigert [14] conducted both in the same central European climate Switzerland and Austria respectively shows interesting results. Both studies had a large number of patients in a similar time frame. Wunder having 7368 IVF cycles from 1995-2003 in Switzerland [9]. Weigert having 8184 IVF cycles from 1992-1999 [14].

Wunder found no statistical significance in implantation and pregnancy rates between seasons, while Weigert found a better pregnancy rate in December. Stolwijik's [5] study in the Netherlands which also had quite a similar climate also reported a better fertilisation and pregnancy rate in the winter season as well. November- February. These findings are difficult to explain, especially in such large studies conducted in very similar climates. Once might say it is coincidence.

One theory for seasonal fluctuations in fertilisation and pregnancy rates is the relation between melatonin and the hypothalamic-pituitary output, neurotransmitters and melatonin are suspected to be related. The seasonal variation in human fertility has been linked to melatonin [15-17].

However its role is still largely unknown up until now. However these studies show that the melatonin influence on the light/dark cycle on female reproduction would mean a decrease in pregnancy rates which is in direct contradiction to this study and Wunder, Weigert and Stolwijik, which had best pregnancy months in winter.

Our results showed that the statistically significant variables influencing the outcome of an IVF cycle are age, etiology of infertility, day of transfer and centre. This concurs with the assisted reproductive technologies data report of 2002 (http://www.cdc.gov/reproductivehealth/ART02/PDF/ART2002.pdf), conducted by the Centers for Disease Control.

In conclusion we maintain that the direct factors that affect outcome are age, etiology of infertility, and centre. However, the suspected seasonal variability for ICSI outcome has not been confirmed with all these studies with differing conclusions: There is no statistically significant variability in fertilization, implantation or pregnancy rates between the seasons in ART. A change of fertility treatments based on seasons should not be taken into account.

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