

## SEASONAL VARIATIONS IN OOCYTE AND EMBRYO RETRIEVAL DURING *IN VITRO* FERTILIZATION: A REVIEW

RASOOL, A.\* AND SARATH, T.

Department of Veterinary Gynaecology and Obstetrics, Tamil Nadu Veterinary and Animal Sciences University, Chennai, India. E. mail: [mirakhter1312@gmail.com](mailto:mirakhter1312@gmail.com)

**Abstract:** *In recent years, in vitro fertilization (IVF) and its associated technologies have demonstrated remarkable advancements. This assisted reproductive technique holds the potential to achieve a greater number of oocytes or embryos collected from donor and higher conception rates. Utilizing elite female donors for oocyte retrieval can also facilitate the production of offspring of the desired sex through IVF. In humans, this technique can be employed to produce offspring in individuals with low fertility or reproductive tract diseases. However, several factors have been identified that can potentially diminish the overall conception rate. These factors encompass reduced fertility, advanced maternal age, nutritional considerations, seasonal variations, and compromised oocyte or embryo quality. This review aims to elucidate the potential influence of external factors, specifically seasonal variation, on oocyte and embryo recovery rates.*

**Keywords:** In vitro fertilization, Pregnancy rate, Oocyte, Embryo quality, Seasonal effect.

### INTRODUCTION

Over the past few decades, scientific and technological advancements in the field of reproduction have led to the development of a wide range of tools and techniques, with Assisted Reproductive Technology (ART) being one of them. IVF was initially introduced for cases involving subfertility, tubal occlusion, utero-tubal pathology and ovulation failure in humans [1]. In domestic animals, the primary objective of using ART is to utilize the female donor of high genetic merit and disseminate superior germplasm [2]. In *in-vitro* fertilization, embryos can be retrieved from individuals with reproductive tract abnormalities that impede normal oocyte or embryo development and gamete transport. Subsequently, these embryos can undergo development and maturation outside the reproductive tract before being transferred to recipients with a normal reproductive tract [3]. Broadly, *in vitro* fertilization

comprises distinct phases: oocyte collection, *in-vitro* oocyte maturation, *in-vitro* fertilization of oocytes, *in-vitro* culture of embryos, cryopreservation of embryos, and embryo transfer [4]. The success rate of IVF depends on numerous factors, beginning with the selection of both donor and recipient and extending to the final embryo transfer. Additionally, the efficacy of various methods utilized in IVF varies. For instance, transvaginal oocyte collection has shown better efficiency compared to other techniques [5]. The success also hinges on the appropriate media for oocyte maturation and external factors that can influence oocyte retrieval and embryo developmental competency. Prior to IVF, both the donor and recipient are subjected to a comprehensive fertility assessment. This includes a gynecological examination, reproductive ultrasonography to identify any reproductive tract abnormalities, tests to ascertain normal ovulation, supplementary assessments to determine ovarian follicular reserves, and a semen

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This work is dedicated to Dr P.D. Gupta on his 85<sup>th</sup> birth day.

analysis for male individuals [4]. Decreased follicular reserves have been linked to a lower oocyte recovery rate, a reduced number of embryos, and an overall decrease in pregnancy success rates. Consequently, this diminished reserve stands as a key factor contributing to unexplained infertility. The effect of seasonality on IVF is not reported clearly, and few conflicting reports have been published.

#### **Seasonal factors influencing IVF:**

Various authors have reported the influence of seasonality on oocyte and embryo quality [6-10]. However, there are differing perspectives, with some authors not considering seasonality as a relevant factor in a high-quality IVF program for humans [11-15]. Furthermore, studies have indicated that seasonal variation can impact semen parameters and subsequently affect conception rates [16-19]. Specifically, during the summer season, semen quality has been found to be notably diminished, potentially resulting in a reduced rate of IVF success [20]. In winter and spring, total sperm per ejaculate and sperm concentration was reported highest. Additionally, the highest percentage of motile sperm was recorded during the spring season [21].

Impact of season on oocyte retrieval and maturation has been documented in various animal species. Studies have reported significant seasonality effects on oocyte and embryo quality in monkeys [22], cats [23,24] and cows [25]. This phenomenon is believed to be linked to a mechanism where reduced steroid hormone production during periods of summer heat stress can compromise oocyte development [26,27]. In humans, the biological mechanism by which seasons influence reproduction remains unclear. Some authors have suggested the involvement of melatonin in oocyte retrieval during seasonal variations [28]. In long and dark winters, reduced ovulation rates, lower embryo quality rates, and an overall decrease in conception rates have been observed compared to the spring and summer seasons [29,30]. Melatonin and vitamin D influence the IVF outcomes by enhancing oocyte maturation and endometrial receptivity. Melatonin exerts a positive impact on oocyte maturation through its antioxidative, autocrine, and paracrine activities. However, it remains uncertain whether melatonin production within follicular granulosa cells and the oocyte itself exhibits the same seasonal variations

[18]. Additionally, animal studies propose that vitamin D stimulates the expression of calcium-binding protein (CaBP28k) in the testes, a protein involved in the processes of spermatogenesis and steroidogenesis [31].

However, as noted by Revelli et al. [12], seasonality does not seem to significantly affect ovarian responsiveness to gonadotropins, the quality of gametes and embryos, or the processes of fertilization and implantation. Similarly, Carlsson et al., [32] demonstrated that when planning and performing IVF/ICS, season should not be taken into consideration.

A recent research by Sebastian et al. [33] suggests that the season can indeed have a potential impact on oocyte recovery rates and overall pregnancy rates. The researchers reported a 30% higher conception rate for oocytes collected during summer compared to winter, with a conception rate of 26%. Likewise, they noted a 28% increase in conception rates for oocytes collected during daytime with the most sunshine, in comparison to the dark period. Therefore, further research is warranted to unravel the full spectrum of influences exerted by seasonality on IVF outcomes.

Several studies have shown that pregnancy rate increase when IVF was performed during longer daylight length, that is during spring and summer, and vitamin D and melatonin is thought to play a major role [6,10]. Some studies support association of vitamin D with reproductive physiology [34,35] and association of Vitamin D in IVF success rate [36]. Contrarily to the above studies, Cozzolino et al. [37], systemic review and meta analysis data showed no correlation between vitamin D and IVF success rate. Similarly, according to Carlsson et al. [32], there is no association between longer sunlight exposure with higher vitamin D levels and pregnancy rate in IVF. A recent breakthrough by Sebastian et al. [33] indicates the potential impact of seasonality on oocyte recovery rates and overall pregnancy rates. When considering the male factor, sperm parameters can undergo significant alterations due to changes in environmental conditions and seasonal variations. This consensus is evident in major studies [16-19]. It is crucial to highlight that the variation in seasonal patterns of oocyte retrieval rates and pregnancy outcomes appears to be entirely different between humans and

animals. This distinction arises from the dissimilarities in ovulatory cyclicality patterns between humans and animals. Also, animal studies are frequently conducted under controlled standard conditions, while as, human studies lack this controlled environment [12]. This distinction underscores the complexity of extrapolating findings from animal research directly to human reproductive processes.

## CONCLUSION

In conclusion, seasonal variations in oocyte and embryo retrieval during in vitro fertilization (IVF) underscores the complex interplay between environmental factors and reproductive outcomes. While studies have shown mixed results regarding the influence of seasons on IVF success, it is evident that various external factors can impact fertility parameters. Seasonal effects on oocyte and embryo quality, as well as sperm parameters, have been explored, highlighting potential associations with melatonin and vitamin D. However, it is crucial to recognize that many other factors, such as age, nutrition, and underlying health conditions, significantly contribute to the overall success of IVF. As the field advances, long-term studies are necessary to establish conclusive findings and comprehend the intricate relationship between seasonal variations, reproductive biology, and assisted reproductive technologies.

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