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ELEVATION OF PROGESTERONE IN DAY OF TRIGGER IN IVF ICSI CYCLE

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Abstract:

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Objective

The main aim of the research is to carry out an analysis that determines the subject about elevation of progesterone in day of trigger in IVF ICSI cycle.

Data Sources

Numerous studies have been considered to investigate the elevation of progesterone in day of trigger in IVF ICSI cycle. However, the following constraints have been defined before consider any data sources for the given research. First and foremost is to define the publication year of the journal. It is important for the authentication of the study to consider relevantly advance sources to avoid any kind of ambiguity regarding the rejection of research. Hence, considering the given circumstances, the data was obtained from various journals that were published between the years 2010 and 2021. The researcher does not aim to go beyond the last decade and value those data sources which are relatively new. Apart from that, it only considers mostly the medical journals. The indexing terms have been used for the selection purpose of the data sources (Lohner, Toews, and Meerpohl, 2017). As the research suggests that it investigate the elevation of progesterone on the day of trigger in the IVF ICSI cycle. Hence the key terms were "progesterone", "elevation of progesterone", "IVF", "ICSI" and "IVF ICSI".

In continuation of previous information, numerous articles have been found which focuses on the following key index terms. These immense amounts of data sources require further segregation to limit the number of journals because it consumes a lot of time for the researcher to read through every article. Therefore, the following segregation has been achieved by the selection of the database of those journals. By considering the reliability and variation of the research, the researcher further segregates the number of journals based on three databases. The following task has been achieved by focusing on Science Direct, Emerald, Brazilian Journal, and Springer as the main source of the database. To sum up the whole discussion, the data sources under the given research are based on those articles which are published within the last decade and affiliated with the given three databases.

Selection of Studies:

In continuation of previous information, it has been mentioned that the type of data sources has been accumulated for the given research topic. The systematic review technique has been applied to the selected journals to determine which of the following published paper is relevant to address the objective of the research (Davies et al., 2017). The researcher read the title of every research and if it seems applicable then the researcher carefully read the abstract of all those articles. The main reason behind this is to make sure whether the particular research topic coincides with the research objectives. Based on these given directions, the inclusion and exclusion criteria have been decided and many types of research have been excluded from the data source. Hence in the end the researcher ends up with 10 published articles. So, in a nutshell, 10 studies were reviewed based on a systematic technique that helped in reviewing the studies based on the elevation of progesterone a



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day of trigger in IVF ICSI cycle. The inclusion criteria that were opted for the study was that the researcher utilises 8 articles that were based on the criteria of the research and were relevant to the research topic. The inclusion criteria were based on the articles published from 2010 to 2021. However, various studies were excluded due to irrelevance and were ineligible for the current study. The studies that do not include content regarding progesterone and IVF/ICSI cycles were excluded. The study excludes conflicts of interest; however, the results of the study may be conflicting.

Data Collection

The data was collected using secondary resources where various studies and literature were used for reviewing the literature. The data was gathered through various online websites, past researches, articles, books, and case studies. The data was collected from different journals including Science Direct, Brazilian Journal, SciELO, Springer, and JSTOR. The purpose of the data collection was that it helped in gaining information and knowledge regarding the elevation of progesterone on the day of trigger in the IVF ICSI cycle.

Data Synthesis

The method that was used for obtaining the results was based on a systematic review. From which the results that were obtained indicated that there is a significant elevation of progesterone on the day of trigger in IVF/ICSI cycle was recognised which determines that the increased the progesterone would be less would be the chances of conceiving a pregnancy. The results determine that more FSH-stimulation could also be the cause for progesterone elevation.

Conclusion

The overall research intended to determine the cause of the progesterone level that helps in maintaining pregnancy. Whereas, it illustrates that the fluctuation in the progesterone rates is reflected in pregnancy. It concludes that there is an immense link between IVF and progesterone which indicates that when there is IVF, a high level of progesterone is indicated due to which there are fewer chances of conceiving a pregnancy.

Keywords: Progesterone, IVF, ICSI cycle, ART, Embryos, Progesterone elevation, etc.

INTRODUCTION

The outcome of the assisted reproductive techniques (ART) is dependent on both the aspects of clinical patients forms and embryo cleavage and growth. The current study is based on exploring and investigating the subject regarding the elevation of progesterone on the day of trigger in the IVF ICSI cycle. The main objective of the literature is to identify the methods that are involved in the study and how it determines the interrelation between the progesterone and ICSI cycle. It provides justification and rationale behind conducting the study which fulfils the identification of the elevation of progesterone in a day of trigger. In this process, the study is searching for the success predictors of increased complexity ART, IVF, and ICSI cycle. It has been observed that several studies have been conducted in this regard which reports a rise in serum progesterone levels. Several studies show that there is a connection between IVF and progesterone which determines that when there is IVF though, there is a high level of progesterone

where there are fewer chances of conceiving pregnancy (Women's, N.C.C. and Children's Health, U.K., 2013). Progesterone is a hormone that generally occurs naturally in the body. Although, it can be developed in the laboratory as well (Cable, and Grider, 2020). The products that are involved in it are Crinone and Prometrium that is formed from a chemical known as diosgenin which is inaccessible through wild yam and soy (Taraborrelli, 2015). Over-the-counter (OTC) progesterone products do not comprise progesterone concentrations as categorised.

Progesterone is a hormone that is free from the ovaries. The change in the progesterone levels could participate in abnormal menstrual periods along with causing menopausal symptoms. It is also essential for the establishment of fertilised eggs that are formed in the uterus and for maintaining a pregnancy (Park, Jee, and Kim, 2015). In vitro fertilisation (IVF) is one of the kinds of assistive reproductive technology (ART) which involves repossessing eggs from the ovaries of women and making them fertilised with sperm. However, the



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fertilised eggs are called an embryo, although, this embryo can be stored which can then be transferred to a women's uterus. During IVF, the eggs that have been matured are gathered from ovaries and are fertilised by sperm in a lab. The complete cycle of IVF comprises three weeks. With the help of IVF, the progesterone levels become high (Ganaie, et al., 2018). However, when the level of progesterone is high, the chances of pregnancy are reduced in fresh transfer. Thus, the reason for this early progesterone increase is still uncertain, hence, the current information advises that improved ovarian stimulus could be the reason for it.

ICSI is also part of IVF, the difference between the two is how the sperm inseminates the eggs. In ICSI the sperm that is selected are directly injected into the egg. According to the studies conducted, it has been revealed that ICSI claims to have a pregnancy success rate of 24% (O'Neill, et al., 2018). While IVF without ICSI has a higher pregnancy rate than 27%. There are two types through which an egg may be fertilised by IVF including outdated and ICSI. In vitro fertilisation (IVF) pregnancies, there is no need of routine fetal echocardiogram evaluation until there is an indication of other risk factors. The study determines that the incidence of congenital heart defects (CHD) are not distinct between IVF and baseline rates of population which has been revealed through the findings of Fertility and Sterility. It has been observed that a fetal echocardiogram was performed in 2230 IVF pregnancies out of which 2040 does not indicate any known risk factors for CHD. However, researchers reported that a mean gestational age pf 22.2 \pm 1.4 weeks at screening time. Therefore, 21 cases were found clinically insignificant due to ventricular septal defects.

On the other hand, several studies reveal that a serum progesterone level that is more than 1.5 mg/ml on the day of trigger day is accountable for the early luteinization that is linked with a decreased rate of pregnancy (Merviel, et al., 2021). For conceiving pregnancy, one possible treatment option is IVF/ICSI sperm injection that can help in fertilization. The results determine that IVF/ICSI has possessed over around 8 million births of children since the year 1978, though, the rate of pregnancy each embryo that is transferred differs from 10 to 50%. Analytical aspects for the pregnancy involve different aspects such as the age of the woman, the number of effective value embryos, and the cycle rank. In the starting, IVF/ICSI was comprised of cleaved embryos that were transmitted on the second or third day (Zhu, et al., 2020). Although, the progression in vitro culture and embryo was cryopreservation that has created the

possibilities of envisaging blastocyst transmission on the fifth or sixth day. There was numerous metaanalysis which indicates that the transfer of blastocyst is linked with higher clinical pregnancy along with increased birth rates (Abuzeid, et al., 2017). Whereas, there are several cases where, cleaved embryos are unable to develop into blastocysts in vitro, thus different couples could attain rudiment implantation earlier.

Moreover, it has been identified that high progesterone has a significant effect on the quality of egg the major concerns are regarding the elevated progesterone which is affiliated with the quality of embryos that were raised in 1993 and 1994. The initial findings determines that elevated serum progesterone level on the hCG administration day has no negative impact on the oocyte's quality and on the outcomes of embryos (Huang, et al., 2016). Furthermore, it shows that the stimulation of protocols has no significant influence on IVF though, it is a poor choice that tends towards diminished egg quality or on the complication on health. It is therefore an unsuccessful IVF consequence that could be accredited in utilizing wrong type of treatment. On the other hand, it has been revealed that the elevated progesterone levels impact fertility at the time of trigger that possess towards decrease in successful cycles. The study indicates that increased progesterone level could make it more difficult for embryos to insert. Whereas, new findings illustrate that physicians recommends that patients that have high level of progesterone level at egg retrieval freeze their embryos and delay for the consequent cycle to be transferred (Ben Rafael, 2020)

METHODOLOGY

The method comprises material and procedures that are implemented in the research. The following research makes use of systematic literature that encompasses 8 literatures that are selected from various journals.



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S.No.	Author	Title	Research Objective	Research Methodology	Research Findings
1.	Merviel, et al., (2021).	Progesterone levels on the human chorionic gonadotropin trigger day affect the pregnancy rates for embryos transferred at different stages of development in both general and selected IVF/ICSI populations	The goal of the study is that it is a retrospective study that helps in examining either the transfer of blastocyst possesses towards increased rates of pregnancy than cleaved transfer of embryo on 3 rd day in both. It analyses the overall and opted IVF/ICSI inhabitants along with the progesterone level of serum affected by the rate of pregnancy.	The technique that has been used was by studying IVF/ICSI cycles with GnRH antagonist -	The findings illustrates that the alterations among the transfer of day 5 embryo (blastocyst) and other embryo groups were found insignificant. The POI and the PFI seems to include prognostic worth for cleaved transmissions of embryos.
2.	Oliveira, et al., (2017).	Progesterone level on the day of hCG administration in relation to the pregnancy rates of patients undergoing assisted reproduction techniques	To examine the prognostic volume for pregnancy of the level of progesterone on managing human chorionic gonadotropin day, where women submitted to aided generative methods.	The research utilises experimental study with 914 women submitted to helped procreant methods from August 2014 to June 2016.	The results shows that the entire pregnancy rate was 34.58%; where pregnancy rate in women aged 38 years was, respectively, 42.3%, 38.7% and 16.1%. For the transference of embryo in similar cycle, and progesterone of 1.3ng/dL, sympathy was 4.78%, specificity, 84.18%, accuracy, 56.72%, positive probability ratio of 0.3019, and negative likelihood ratio of 1.1312, with the one who receives working



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					distinctive arc of 0.46 (95%CI: 0.42-0.49).
3. Lawre & Fa (2017	temi,	Effect of progesterone elevation in follicular phase of IVF-cycles on the endometrial receptivity.	The impact of preeminent outlying progesterone levels in the late follicular phase that appears to be on the endometrium along with the opening of imbedding, that leads towards asynchronism among the endometrium and the emerging embryo.	The method that was used for the study was to determine the progesterone level that tends towards representing critical threshold, where an adverse impact on the continuing pregnancy rate in fresh IVF cycles were detected.	The findinsg of the study demonstrates that the reasons that were identified for premature elevation of progesterone throughout ovarian stimulation were still not clear; whereas, current studies highlighted towards improved FSH-stimulation as the major reason for the elevation of progesterone.
4. Huan al., (2016	g, et	Elevated Progesterone Levels on the Day of Oocyte Maturation May Affect Top Quality Embryo IVF Cycles	The goal of the study is to examine the rate of TQE significantly that are connected with progesterone concentration on the day of human chorionic gonadotropin injection day. It determines the levels of progesterone on the day of oocyte maturation.	The methods that were utilised for the preparation of sperm, IVF and embryo culture. The oocytes were nurtured in G-IVF medium (Vitrolife) and inseminated 3 to 4 hours after recovery.	The findings that were examined shows that 4,236 fresh IVF cycles evidently shows an adverse influence of raised progesterone levels on hCG trigger day, along with TQE rate that is irrespective of the basal FSH. The overall gonadotropin is relied on woman age, or the period of ovarian stimulation.
5. Vikas Swati (2017	,	The Impact of Progesterone Level on Day Of hCG Injection in IVF Cycles on Clinical Pregnancy Rate.	The objective of the research was to assess the occurrence of PPR on trigger day	The purpose of the literature was to analyse the prevalence of	The entire rate of clinical pregnancy of each embryo



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			in conservative IVF/ICSI cycles and its influence on clinical pregnancy rate.	of induction in predictable IVF/ICSI cycles and its effect on the rate of clinical pregnancy. The method that was utilised was based on testing PPR induction.	transmission was 30.6%. The medical rate of pregnancy in the patients with P ₄ <1.5 ng/ml was found significantly advanced than those with raised levels, P ₄ ≥ 1.5 ng/ml (33.3% vs. 12.9%; P = 0.037). Early progesterone advancement in ART cycles is probably linked with inferior clinical pregnancy rates.
6.	Esteves, et al., (2018).	Association Between Progesterone Elevation on the Day of Human Chronic Gonadotropin Trigger and Pregnancy Outcomes After Fresh Embryo Transfer in In Vitro Fertilization/Intracytoplasmic Sperm Injection Cycles	The goals of the study are to examine the Progesterone elevation (PE) during the late follicular stage of measured ovarian inspiration in fresh transfer of embryo in vitro fertilization (IVF)/intracytoplasmic sperm injection cycles which has been has been demanded to be linked with minimised rates of pregnancy.	The method that was identified was affiliated with poorly agreed on the outcomes due to less evaluation specificity, poor optimisation of techniques over the huge attentiveness which ranged from observed clinically, and insufficient calibration.	A possible contrary impact of PE on pregnancy achievement do not appears to impact on entire population of the patient equally, with high respondents to COS being less vulnerable to the conceivable harmful influence of PE.
7.	Wu, et al., (2019).	Progesterone elevation on the day of hCG trigger has detrimental effect on live birth rate in low and intermediate ovarian responders, but not in high responders	The purpose of the research is to make comparison of the impacts of PE on the hCG trigger day on live birth rates (LBs) in little, middle and high respondents of the ovarian and to examine the deadline value for PE in distinct populace on	The study utilises various statistical methods, several characteristics of the patients were enlisted, and the reflective nature of studies investigating the association among PE and clinical results.	The findings shows that our multivariate assessment exhibited that LH and E2 levels on hCG trigger day were in relation with PE in the entire ovarian respondents



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				the basis of the responses of ovarian,		groups. The LH and E_2 levels
				we look back to		on the day of
				assess 2,351 patients		hCG trigger
				in total that receives		were evidently
				fresh ART transfer		advanced in
				cycles with GnRH		the PE group
				agonist utilising an		instead of non-
				extended or petite		PE group.
				procedure.		i L group.
8.	Lawrenz,	Premature	progesterone	The objective is to	The method that	The outcomes
0.	et al.,	elevation: targets		examine the	was utilised was	of the research
	(2018).	strategies	ana reseac	premature	of examining the	illustrated no
	(2010).	Strategies		progesterone	endometrial	alterations in
				elevation that targets	samples by	terms of
				and release tactics.	applying	imbedding,
					parametric	pregnancy and
					method.	the rates of
						miscarriage
						among the
						receivers that
						obtains oocytes
						from the series
						in which P was
						high
						(≥1.2 ng/mL)
						and individuals
						who attain
						oocytes gained
						in the sequence
						with P under
						the edge.

PRISMA FRAMEWORK

PRISMA is the flow diagram that aids in portraying the data flow via various stages. It is the method that is mainly utilised in the systematic review. It outlines records that are observed, excluded, and included along with the causes for their inclusion and exclusion. The following is the PRISMA flow diagram which demonstrates numerous studies that are involved in the literature.

It could be seen that two major databases are involved which include Google Scholar and Science Direct. With the utilization of inclusion and exclusion criteria, it could be observed that the following studies were excluded based on their topics and the abstract that fulfill the requirement of the present study. After this exclusion, 10 articles were screened based on the eligibility criteria. Thus, several articles were excluded for various reasons that led towards opting for articles for analysis in the current study.

RESULTS

The empirical review of the studies was undertaken. 8 articles were observed and reviewed in the study. However, the results that we come across through those articles were that the transmission of the blastocyst are linked with advanced scientific pregnancy and the rates of birth than cleaved embryo transference in the overall populace were opted from the overall population. Thus, on the day of progesterone levels on the day before trigger day predicted to be on the likelihood of pregnancy. It identifies that there are various couples that consults for infertility that fails to attain pregnancy through sexual intercourse. However, it shows that the transfer of blastocyst has various advantages that helps in minimising uterine exposure to very increased serum estradiol levels. The demographic and clinical statistics over the entire populace are summarized as the existence and lack of pregnancy through embryo transfer phase. The findings of other study determines that the women pregnancy rate vary according to the transfer of embryo in the cycles and progesterone



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level. It shows that human chorionic gonadotropin varies according to prognostic capacity for pregnancy in patients. The findings determine that the level of progesterone seems to be reflecting based on the critical threshold which has a negative impact on the ongoing pregnancy rate where IVF cycles have a potential effect that is observed. Hence, the other study contradicts on the association among the progesterone elevation in fresh cycle and on the probability of pregnancy after the transference of frozen embryos were formulated from that cycle. Moreover, more developed FSH-stimulation could also be the source for the elevation of progesterone.

Another study determines that medical pregnancy was referred to as the existence of gestational sac through fetal heart activity and the analysis of ultrasound through the retrieval of oocyte. The results determine that the level of elevated progesterone before oocyte development were continuously harmful to the oocyte. Thus, the instrument through which the elevated progesterone level becomes the reason for negative impact has not yet been explored. The result of another study explores that the cancellation of cycle and embryo freezing should be individualized based on the quality and number of embryos and early detection of the increase of P4 tends towards attaining effective success rates in IVF. The study was based on conflicting evidence that prevails concerning the impact of P elevation on the day of hCG trigger in fresh embryo transfer of IVF/ICSI pregnancy outcomes. It shows that a potential negative effect of PE on the success of pregnancy was not found to impact the entire population of patients. Another study identifies that PE has unfavorable influences on LBRs in low to middle ovarian responders thus Vitro fertilization could be optimized through the treatment of IVF/OCSI patients.

DISCUSSION

The aim of the present research was to assess the elevation of progesterone on trigger day in IVF/ICSI cycles that tends to be the predictive tool for pregnancy rate. The adverse effect on conceiving pregnancy of women could base on individual's age, stimulation parameters, duration of infertility and the number of embryos transferred. The following elements counts as a potential aspect in patients' pregnancy.

The discussion conducted determines that higher level of estrogen, intermediate follicles were found on trigger day that are linked with premature progesterone elevation in the study. Moreover, the LH level on trigger day might be affiliated with plausible explanations that could be in favor of the current situation. The premature P_4 elevation was increasingly

found in the patients. The comparison of progesterone level and ICSI cycle demonstrates that there is an increased need for the level of progesterone for establishment where the level should be in between 10 and 20 ng/ml that could help in increasing implantation and continuing pregnancy rates for the single use of embryos. Moreover, the studies determines that the progesterone level increases during luteal phase of the ovarian cycle and the secretory stage of uterine cycle. It shows that menstruum happens when the progesterone level is dropped. A progesterone level that is above 3 reveals that the ovulation has occurred and at level 10 it suggests adequate production for maintaining pregnancy. The levels of progesterone are used for monitoring treatment where the levels targeted could be higher and these targets could vary among fertility clinics. As discussed in the study, it shows that IVF/ICSI has possessed more han 8 million babies gave births from 1978, though, rate varies around 10-50%.

It has been observed through the studies that various levels of progesterone remain elevated throughout pregnancy. The following elevated levels possess towards preventing the body from producing more eggs at the time of pregnancy. The production of progesterone is generally the sphere of the ovary until placenta takes over progesterone manufacture in 8-10 weeks of gestational age. Thus, the level of progesterone on human chorionic have no effect on clinical pregnancy due to vitro fertilization. The progesterone comcentration in between 1.0 and 1.25 ng/ml tends towards resulting in good clinical pregnancy results.

CONCLUSION

The existing study intends to highlight on examining regarding the elevation of progesterone in day of trigger in IVF ICSI cycle. The study determines that the cancellation of cycle and embryo freezing should be individualized based on the quality and number of embryos and early detection of the increase of P4 tends towards attaining effective success rates in IVF and in elevating progesterone level. It concludes that the change in the progesterone levels could participate in abnormal menstrual periods along with causing menopausal symptoms. Thus, it further determines that the level of elevated progesterone earlier oocyte maturation was continuously detrimental to the oocyte. Conclusively, it illustrates that progesterone concentration the day before the day of the trigger are foreseen to be on the likelihood of pregnancy. In addition, the level of progesterone seems to be reflecting based on critical threshold which has an adverse impact on the ongoing pregnancy rate where IVF cycles hsave a potential



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effect. Hence, the study concludes that more developed FSH-stimulation could also be the cause for progesterone elevation.

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