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Risk Factors Associated with Maternal Age and Other Parameters in Assisted Reproductive Technologies - A Brief Review

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ABSTRACT

Assisted reproductive technology is advancing at fast pace. Increased use of ART (Assisted reproductive technology) is due to changing living standards which involve increased educational and career demand, higher rate of infertility due to poor lifestyle and child conceivement after second marriage. This study gives an overview that how advancing age affects maternal and neonatal outcomes in ART (Assisted reproductive technology). Also it illustrates how other factor like obesity and twin pregnancies complicates the scenario. The studies find an increased rate of preterm birth .gestational hypertension, cesarean delivery chances, high density plasma, Preeclampsia and fetal death at advanced age. The study also shows the combinatorial effects of mother age with number of embryos along with number of good quality embryos which are transferred in ART (Assisted reproductive technology). In advanced age women high clinical and multiple pregnancy rate is achieved by increasing the number along with quality of embryos.

Keywords: Reproductive techniques, Fertility, Lifestyle, Preterm delivery, Obesity, Infertility

INTRODUCTION

Assisted reproductive technology actually involves group of treatments which are used to achieve pregnancy when patients are suffering from issues like infertility or subfertility. The treatments can involve invitro fertilization [IVF], intracytoplasmic sperm injection [ICSI], embryo transfer, egg donation, sperm donation, cryopreservation, etc., [1]. First IVF infant was born about 30 years ago. Since that assisted reproductive technology has advanced at fast pace [2]. Although IVF, ICSI and other assisted reproductive technologies are widely used now days in major portion of the world but risks associated with them cannot be neglected [3]. This is under discussion that whether the complications faced in assisted reproductive technologies are because of used technique or advanced maternal age or some other maternal parameter like oocyte quality or fertility [4]. Advanced age pregnancy can be due to number of reasons higher education for extended period of time, increased career demand, child conceiving in the second marriage, etc. [5]. ART is nowadays used in achieving pregnancies in women aged more than 35 years including women more than 45 years. The review is being written in contest to assess whether ART is associated in producing adverse birth effects like early delivery in pregnancy, low birth weight, preterm delivery, very low birth weight, presentational diabetes and gestational diabetes etc. and how the age factor is playing its role in this. More recently studies showed increased risk of these factors in ART as compared to spontaneous conception SC [6]. Amongst risk factors Preterm birth is attributed as premature birth which can be either less than 37 weeks or even less than 32 weeks. This can lead to cerebral palsy, sight problems, hearing problems, delays in development [7]. If newly born weighs less than 2499 g it is called as low birth weight LBW while less than 1500 g is called as very low birth weight and less than 1000 g is termed as extremely low birth weight ELBW [8]. If type 1 or type 2 diabetes existed before conception this is termed as pre gestational diabetes. While gestational diabetes [GD] is glucose intolerance which is diagnosed during pregnancy. Some maternal factors can be cause of this GD which may result in depression, preeclampsia, jaundice, cesarean birth and in worst cases stillbirth [9].

EFFECTS OF MATERNAL AGE ON MATERNAL OUTCOMES

Risk of high density plasma HDP is higher in ART pregnancies and is higher as compared to SC at 25-30 years of age and significant increased rate observed from 35-40 years in ART. Risk of placental abruption is higher in ART as compared to SC but does not increase significantly with advancing age in ART. The risk of placenta previa is higher in ART and increases with age till 30 years. Caesarian delivery chances are more in ART as compared to SC and increase in both with advancing age [10].

EFFECTS OF MATERNAL AGE ON NEONATAL OUTCOMES

Less than 37 weeks preterm birth PTB risk is higher in SC as compared to ART, for women aged greater than 35 years. While less than 32 weeks PTB risk is same in both SC and ART for more than 35 years of age. LBW and VLBW is higher in ART as compared to SC. while in contest of age, risk in ART decreases up to age 30 then becomes constant meanwhile it increases above age 30 in SC.

Small for gestational age SGA is higher in ART at age 25-30 years and has low risk factor from 40-45 years of age. For women less than 35 years risk of macrosomia is lower in ART as compared to SC and does not change for increasing age in ART singletons. Perinatal mortality rate is higher in ART at age 25-30 years and does not increase further with advancing age [10] (Table 1).

EFFECTS OF MATERNAL AGE IN TWIN PREGNANCIES

During twin pregnancies Risk of previous miscarriage and pre gestational hypertension is higher in women above 35 years. While no risk difference found in pre gestational diabetes and BMI.

Evaluating PB, in twin pregnancies after ART, a trend of higher rate of total PB rate within mother aged ≥ 40 years old observed. However, mothers aged under 35 years showed higher rate of SPB <37 weeks and <32 weeks, whereas mothers ≥ 40 years old showed significantly higher rate of iatrogenic PB <37 weeks of gestation. Nevertheless, maternal and fetal indications for iatrogenic PB <37 weeks and <32 weeks were not significantly different across different ages [11] (Table 2).

EFFECT OF MATERNAL AGE IN ONSET OF CANCER AFTER ART

Among women who undergone ART, those who were diagnosed with cancer were relatively older at the start of ART treatment (37.8 years vs. 35.3 years). Types of cancer observed are endocrine, melanoma, ovarian, breast, uterine, genital including cervix, uterus, female genitalia, vagina and vulva [12] (Table 3).

Table 1: Maternal age effects in ART-maternal and neonatal outcomes

	Risk factor	Age 25-30 years	Age 35-45 years
Maternal outcomes	HDP Placental abruption Cesarean delivery chances	Reduced rate of occurrence Steady rate increase till age 30 Less at this age	Increased rate of occurrence No significant increase in rate observed Higher at this age
Neonatal outcomes	LBW/VLBW SGA Perinatal mortality Macrosomia	Risk decreases till age 30 High risk Increase from 25-30 Lower as compared to SC	Rate becomes constant above 35 Low risk At 35 rate becomes constant Lower as compared to SC

Table 2: Effects of maternal age in ART during twin pregnancies

	Risk factor	Age less than 30 years	Age greater than 40 years
In twin pregnancies	Gestational hypertension	Lower	Higher
	Pregestational diabetes	Same like SC	Same like SC
	Preterm birth	Lower	Higher
	BMI	No risk	No risk

Table 3: Effect of maternal age in combination with obesity

	Risk factor	Age<35 years	Age>35 years
Maternal outcomes	Preeclampsia	Low	High
	Cesarean	Low	High
	Preterm delivery	Low	High
Neonatal outcomes	Neonatal intensive care need	Low	High
	Fetal death/still birth	Low	High

EFFECT OF MATERNAL AGE IN COMBINATION WITH OBESITY

In comparison to younger lean women aged less than 35, the preterm delivery rate for <28 weeks of gestation period, pre-eclampsia and cesarean are the most of all in overweight and obese women aged less than 35 years depicting 3 to 4 fold risk in obese women. At 28-31 weeks of gestation the chances of fetal death along with preterm delivery were higher in these women. The combination of overweight or obesity along with maternal age 35 or older can cause an increased rate of preeclampsia, large for gestational age LGA along with preterm delivery less than 28 weeks of gestation period, whereas the chances are doubled as compared to less weight patient of the similar age group. Neonatal intensive care needs increased and fetal death also. Cesarean along with induced births in these women are also observed. In two groups having same BMI where one having women aged above 35 years and 2nd having women aged below 35 years the 2nd group have higher risk of preterm deliveries and fetal death [13].

COMBINATORIAL EFFECTS OF PATIENT'S AGE AND NUMBER OF EMBRYOS TRANSFERRED

If we transfer 1-3 embryos in the patients less than 30 years no marked difference could be observed in clinical pregnancy rate.in addition multiple pregnancies cannot be observed if we transfer single embryo. In the patients between ages 30-35 lower clinical pregnancy rate calculated in the cases where single embryo was being transferred. If we make two groups, in one 2 embryos transferred and in other 3 embryos transferred no significant difference found. Also if multiple pregnancies rate observed not marked deviations observed. In the class of women above 35, rate of clinical pregnancies and rate of multiple pregnancies have positive correlation with the number of total embryos transferred, but not significant differences observed.

COMBINATORIAL EFFECTS OF PATIENT'S AGE AND NUMBER OF GOOD QUALITY EMBRYOS TRANSFERRED

Embryos with blastomeres equal and greater than 3 on the 2nd day of fertilization are regarded as good quality embryos. While on 3rd day of fertilization embryos which are having equal or more than 6 blastomeres are regarded as good quality ones. The morphology score given to them is grade 1 or grade 2. On day 5th of fertilization the embryo which is having score of morphology equal or higher than 3 is regarded as good quality one. Balaban et al. [14] and Deng et al. [15] classified embryos quality in this manner in 2002 and 2004 respectively. If 2 or 3 embryos of relatively good quality are transferred the women with age less than 30 years show quite similar trend of pregnancy rate.it is markedly higher in comparison to the cases where 0-1 embryos of good quality are transferred. If we transfer 2 to 3 embryos in women aged from 30-35 relatively higher clinical pregnancies rate achieved. If we transfer 3 embryos with good quality high multiple pregnancies rate achieved. And in the women above 35 an upward trend for multiple pregnancies occurrence observed if we increase the number of embryos which are to be transferred. And amongst all groups when 3 good quality embryos are being transferred highest rate observed [16] (Table 4).

DISCUSSION AND CONCLUSION

In this review assessment is done about how age affects mother and child in assisted reproductive technology in comparison to spontaneous conception. This is also worked out that how age factor make things worse or better in combination with other factors like obesity, cancer, onset of twin pregnancies, number of embryos transferred, etc. Different cohort study research papers are being taken in consideration to achieve the above mentioned results. Results showed that in advanced age there is increased risk of HDP, cesarean delivery chances and occurrence of macrosomia. While no significant increase observed in SGA. Perinatal mortality, LBW, VLBW and placental abruption. All these factors are reviewed in ART. In addition to this, when obesity and other factors like twin pregnancies and other ART parameters are combined to it this can lead to higher risk of gestational diabetes, still birth increased rate, cesarean delivery increased chances of gestational hypertension, and preterm delivery.

Table 4: Combinatorial effect of age with number of embryos along with number of good quality embryos

		Women aged <30 years	**Women aged 30-34 years**	**Women aged >35 years**
Number of embryos transferred	With increasing number of embryos transferred	No significant change in clinical and multiple pregnancies rate	Relatively lower clinical and constant multiple pregnancies rate	Clinical and multiple pregnancies rate both increases
Number of good quality embryos transferred	With increasing number of good quality embryos transferred	Increased multiple pregnancies rate	Increased clinical pregnancies rate	Increased both clinical and multiple pregnancies rates

The positive aspect of this study is that it summed up data from different cohort study research papers published in the last decade. Critical evaluation and correlation of these studies enabled to illustrate different parameters in single study. Also this illustrates correlation of SC and ART and different trends of different parameters over the entire reproductive age of women.

However the limitation of the study is that data is being recruited from the studies which were based on selective populations and they do not involve the different and exceptional trends of some major populations worldwide. Hence the results may not hold true to certain populations.

Increased fertility problems arising due to changing living standards. Meanwhile, assisted reproductive technologies are also evolving with time and some of their risk factors are also on board. However these risks needed to be overcome to get healthy generations further.

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