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Ocular Changes in Children Born through Assisted Reproductive Technologies: A Review

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Abstract

Assisted reproductive technology is used worldwide to achieve pregnancy for millions of childless couples and help them to give birth to a healthy baby of their own.Many ocular changes and undesirable effects of the techniques used in this procedure were seen in mothers and infants.There is much evidence on the ocular anomalies reported in children born through ART. Studies stated reduced visual acuity, anisometropia, and other ocular manifestations which occur early during the embryogenesis process or it may be related to the risk factors which influenced the development of child during these pregnancies. This review highlights the ocular changes seen in children born through Assisted Reproductive Technologies.

Keywords: IVF(In-Vitro Fertilization), ART(Assisted Reproductive Technology), ICSI(Intra-Cytoplasmic Sperm Injection).

Introduction

World Health Organization(WHO) defined infertility as the inability to conceive after more than one year of intercourse withoutcontraception[1].There are different factors that can lead to infertility in males and females.With the help of Assisted Reproductive Technology(ART) procedures, like fertility medication, artificial inseminationin-Vitro fertilization, Intra-cytoplasmic sperm injection, cryopreservation of gametes or embryos, and surrogacy these infertile couples produce a healthy baby of their own. This technology is considered a safe way to achieve pregnancy. Most pregnancies conceived by ART have healthbenefits except for the increased incidence of premature birth[2].Multiple ART pregnancies result in increased prematurity and its associated complications. It is reported that some ART pregnancies have risks of obstetric and neonatal complications.It can be either the procedure used or the etiology of infertility [3].

The development of the visual system begins early during the embryonic period and continues until after the birth of the child [4].Infants born through ART may be susceptible to several factors with undesirable effects on the development of the visual system [5].The ocular changes and abnormalities associated with ART in women and children are incompletely known, as few studies have been conducted on this topic.

Ocular abnormalities in children born through Assisted Reproductive Technologies:

ART was associated with eye malformations,reduced visual acuity, and also cases of anisometropia [5]. Theseabnormalities may be either secondary to de novo deletions, which occurred early during the embryogenesis process, or can also be related to risk factors that influenced the development of these pregnancies.Manipulation of oocytes and sperm, the medications which are used for ovarian stimulation, the culture medium, and the temperature to which developing embryos are exposed may contribute as risk factors [7].

Evidence of the effect of assisted reproductive technology on ocular assessments of the women undergoing ARTfound that in in-vitro fertilization, 32 women followed until 3 months postpartum showed baseline mean IOP decrement,corneal pachymetry and corneal endothelial cell counts increment from phases V1 to V4 of ART [6]. Studies described effect of ART onocular and visual performances ofchildren and found of having red reflex abnormalities in preterm infants and young males and fixation controlfailure was seen more frequently with increasing refractive error, primarily in preterm infants. The probability of fixation conditions and visual deficiencies is highlighted in ART infants[3,7].Studies also showed that preterm infants are at more risk for developing retinopathy of prematurity, refractiveerrors, reduced Visual acuity, strabismus and amblyopia also reported [3].

Kuiper et al demonstrated that,children obtained through Invitro- fertilization(IVF) with controlled ovarian stimulation protocols were more likely to wear eyeglasses at the age of 11 years when compared to the control group. Several studies also stated that children born through IVF, compared to the general population,with similar risk of visual disturbancescan be due to certain factors like maternal age,parity, smokingstatus, nutritional status,etc [8,9]. Also,it was stated that preterm infants are at risk of Retinopathy of prematurity(ROP),reduced visual acuity,refractive errors,strabismus, and amblyopia [9,10]. An increased rate of refractive errors, including myopia and hyperopiawas found in children born through ART [7,11]. Whereas, another study assessed the risk of auditory and visual abnormalities in the Intra-Cytoplasmic Sperm Injection (ICSI) population.28% of children in the ICSI group were diagnosed with visual impairment compared to 35% in the control group [11,12].

Wikstrand MH et al,found an association between the ICSI(Intra-Cytoplasmic Sperm Injection) and the risk of abnormal retinal vascularization in young males. Authorsconcluded that ICSI alonedoes not increase the risk of ocular abnormalities.There can be association withrisk factors like parenteral characteristics which mayinfluence the ICSI [13]. Medications for ovarian stimulation may cause hypermethylation of RB1 gene promoter whichpartially explains the association between ART and retinoblastoma. Two studies showed that the relative risk of retinoblastoma is high for an estimated IVF birth rate of 1.0%-1.5%. The studies mainly addressedthe need to do early ophthalmological screening in children born through ART [14,15,16,17]. There is an increased incidence of imprinting disorders in children born through ART,Hypermethylation of the rb1 gene causes retinoblastoma [18,19]. In 2001 the first retinoblastoma was found in a child born through IVF and in 2003 another 5 cases were reported by a Dutch study of these five,one appear to be caused by gene mutation, and the imprintingstatus of the rest fourwas not determined [18]. The study concluded that further studies with the imprinting status of the rb1 gene are needed to draw valid conclusions and rule out the association between ART and

retinoblastoma.Lee et al.,through his reports suggested the use of IVF Fertility drugs can be a cause for the development of retinoblastoma but there is a lack of evidence in the association between IVF treatment and cancer development [21]. Another possibility is explained as it can be associated with the culture medium used in the IVF tube. Subtle changes in the ingredients of the culture medium can alter the activities of imprinted gene [22]. Athird possibility can be whichis the inheritance of genetic defects from gametes and embryo trauma while performing ICSI (IVF) [20,21,22].

ART has been an answer to many childless couples, but it always hasmany risks and complications. Many studies stated that complications occur due to multiple pregnancies, premature labor, administration of hormones and drugs, improper follow-up of the patients who have undergone ART, and a wrongfollow-up of the children born through ART.The related risk factors influencing these pregnancies' development can also be related.While considering all the evidence mentioned above, it is evident that children born through IVF has incidences of retinoblastoma,eye malformations,reduced visual acuity, Retinopathy of prematurity, refractive errors, strabismus,amblyopia,red reflex abnormalities, and anisometropia.

Conclusion

Development of the visual system begins early during pregnancy, between 3-10 weeks of gestation. Particular intrinsic as well as extrinsic factors, can influence its actions.The medication used in controlling ovarianstimulations, the technique used in achieving pregnancy,the parenteral characteristics and factors, multiplepregnancies, and prematurelabor can lead to possible complications in infants born through ART and slight ocular changes in the mothers.Thus a detailed ocular evaluation for mother during the phase of ART and children born through Assisted Reproductive Technologies is warrantied.

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