

## Refractive Error and Fixation Conditions of Infants Born by Assisted Reproductive Techniques

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### Abstract

**Background:** The objective of this study is to evaluate the refractive error and oculomotor conditions of infants born by assisted reproductive techniques (ART) in patients referring to Royan Institute as well as Child Health and Development Center.

**Materials and Methods:** In this cross-sectional study, 270 ART-exposed infants aged less than 9 months were tested by retinoscopy, fixation conditions, Hirschberg and Doll's eye maneuver.

**Results:** The average refractive error of these infants shows hyperopic Shift  $+0.9 \pm 1.1$  D. The average astigmatism recorded in these infants is  $-0.6 \pm 0.6$  D. The prevalence of refractive errors in these infants is myopia 6%, hyperopia 85% and emmetropia 9%. Impairment of fixation conditions, Hirschberg test and Doll's eye maneuver was respectively observed in 20.4, 1.4 and 3.7% of the studied infants.

**Conclusion** Given the sensitivities in the visual system development process and critical period which is important for every infant in the very first months of birth, it seems that visual-ocular studies are more important in ART-exposed infants who were exposed to different factors until their birth. The results of refractive errors, fixation conditions, Hirschberg test and Doll's head maneuver which was conducted in this study for these infants reveal that, it is likely that visual impairment in these infants is higher than the results of foreign studies. However, lack of access to population studies in infants below 1 year of age in Iran necessitates more extensive studies and follow-ups of vision of ART-exposed infants more seriously.

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## Introduction

Recent scientific advancements have made it possible to fertilize infertile couples. Scientists and actually, parents of children of such interventions always face questions and concerns of how the visual and ocular health of these children will be. Despite the extensive studies and actions in the field of assisted reproductive techniques, especially in Iran, unfortunately no comprehensive study has been conducted regarding visual and ocular health and different reflexes of visual system of these infants. Given that these infants are born at high costs and after years of treatment, it is determined that why it is so important to evaluate and monitor ART-exposed infants.

Visual system evolutionary process starts during fetal period and will also continue after birth [1]. Appropriate and complete evolution of visual system in human will depend on several internal and external factors [2]. ART-exposed infants may be exposed to several factors which have unintended effects on evolution of the visual system of infants [3]. On the other hand, the conditions of

maintaining infants before and after birth may have effects on their visual system [4]. Thus, awareness of the visual system conditions of these infant can be a base and index to select the assisted reproductive therapy and cares affecting it. On the other hand, the age period of zero to twelve months is considered the critical period [5]. Although in some studies, the development of these reflexes may also continue after three years of age [6]. Appropriate medical actions in this age range can reduce negative effects of disturbing factors of growth and visual system development [7]. Therefore, as a principle in visual sciences, all infants whose growth and development conditions during fetal period have been hazardous and have genetic predispositions in this field, must be under different visual tests during this period [8]. Accordingly, several screening tests have been considered in this age period in different countries [9-11]. These tests include evaluation of refractive error, refractive media, motility systems, binocularity, amblyopia, and internal and external structures of eye [9-11]. Given the

importance of the visual condition of these infants, a study was designed and conducted to examine visual conditions of these infants.

## Materials and Methods

This cross-sectional study was conducted in child health centers affiliated to University Jihad of Iran University of Medical Sciences. Ethical considerations of this study were evaluated and approved in the Ethics Committee of Royan Institute as well as the Central Office of University Jihad. Non-randomized sequential sampling was performed; therefore, according to the arrangements made with Royan fertility center affiliated to University Jihad, the representative of child health and development center and the couples referred to Royan center with couples referring to Royan institute for eye examinations of infants after birth, they were given expanded explanations. Necessary arrangements were made regarding the time of referring parents to the optometry department of child health and development center. The infants referred to the optometry department of child health and development center from the time when they were one month old. At this time, the data on the history and conditions of birth were collected from parents. Clinical ocular examinations of these infants were conducted after three months old. To ensure the initial findings, the same infants were again evaluated at the age of nine months. Then, their refractive conditions were evaluated using static streak retinoscopy through dry refraction method. Considering the examinations in other departments of the child health center, relatively long duration of other examinations conducted by various experts and the time needed for cyclorefraction, and of course most parent's lack of consent for use of cycloplegic drugs, cyclorefraction was not conducted. The mother was holding the infant while fixation evaluations were performed as follows.

At first, focused light was flashed into infant's eyes by a flashlight. Corneal light reflex was assessed from two aspects (Hirschberg test), symmetry and centrality of corneal light reflexes to the pupil center. If possible, and if fixation of infant continued, unilateral cover test would be performed. The quality of the infant's fixation was assessed to ability to maintain fixation by flashlight, eye rotation or fixation wandering and eye drift. According to the age of samples and some studies [12], duration of continuous fixation of the infant's eyes was considered at least 3 seconds for a good fixation. Doll's head maneuver was assessed using appropriate visual stimuli [13]. To conduct this test, the infant was held vertically from armpit by the examiner [14]. The infant's face must be put on surface of the examiner's face. In these conditions, the examiner must hold the infant so that the infant's head and neck would be hold by the examiner's fingers. Then, the examiner and infant rotate 360 degrees together. Observing the infant's eyes, we will realize the infant's eyes rotating reverse to the direction of turning. Nystagmus will be naturally lost in the eyes of infant less

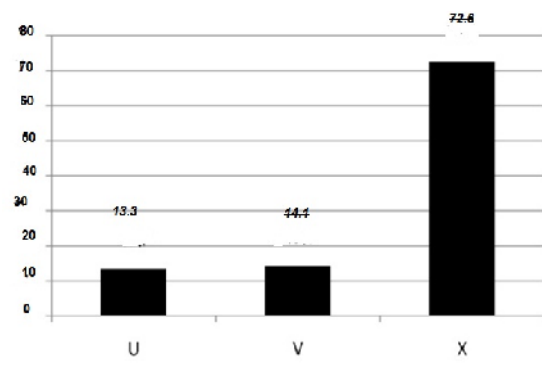
than 5 seconds after the infant's rotation. Some infants failed to do some or all of the tests duration the examination due to their restlessness, crying, sleeping or their parent's intolerance. It was not possible to test all 270 people referred to the Optometry Department of Child Health and Development Center. The referred people were asked to refer to the Optometry Department of Child Health and Development Center again before the age of one year and preferably about nine months. Those who needed more actions or examinations were referred to specialized and sub-specialized centers. The results were analyzed by SPSS-16 software.

## Results

In the first phase of this study, 270 infants were studied 138 (51%) of whom were female and 132 (49%) were male. Assisted reproductive techniques in this study include IUI (intrauterine insemination) 13.3% of cases, IVF (In vitro fertilization) 14.1% and ICSI (intracytoplasmic sperm injection) 72.6. In Figure 1, each of the IUI, IVF and ICSI methods are respectively shown with letters u, v and x. The average age of the studied infants was  $5.1 \pm 3.1$  months and their average birth weight was  $2741 \pm 624.5$  g (1150-4200). Birth weight of most of them was 3200 g.

**Table 1.** Indicators of central tendency and dispersion of values of spherical refractive errors, the right and left eye astigmatism power

|               | left eye astigmatism | right eye astigmatism | left eye spherical error | right eye spherical error |
|---------------|----------------------|-----------------------|--------------------------|---------------------------|
| Mean $\pm$ SD | -0.6                 | -0.6                  | 1.1 $\pm$ 0.9            | 1.1 $\pm$ 0.9             |
| Max           | 0                    | 0                     | -5.5                     | -5.5                      |
| Min           | -2.5                 | -2.5                  | +4                       | +4                        |



**Figure 1.** Assisted reproductive techniques

The results of Doll's head test revealed that 88.5% (239 people) of the studied infants showed normal results. Abnormal results were observed in 3.7% (10 patients). Some of the infants was not ready for test for various reasons (7.8%, n=21). The study of fixation conditions of infants shows fixation abnormality in 20.4% of the

infants. 71.1% showed good results, but this study was not possible in 8.5% of them. Reviewing the oculomotor conditions of infants indicates that 61.9% had favorable conditions, but 0.7% showed exotropia and 0.7% a distinct esotropia. Study of eye movements was not possible in 36.7%.

## Discussion

As seen in the results of this study, hypermetropia (hyperopia) was refractive error of most infants. Some samples of all assisted reproductive technologies used in Iran participated in this study. But the majority of investigated infants were born using ICSI procedures. Various types of visual and ocular disorders observed in these infants showed a very diverse and variable prevalence. Exotropia was observed in 0.7% of them, while 20.4% of these infants did not show a proper fixation. Diversity and difference of these disorders suggest different developmental evolutionary mechanisms in the visual system. Not many years have passed from providing assisted reproductive techniques in the world. Thus, not many reports are seen in scientific sources on visual conditions of these infants. One of the most important studies in this field was the study of Anteby et al [15]. Their study was performed on (82 eyes) 47 females and males of 2 months old to 5 years old that were born through IVF procedure.

In their study myopia was 16%, hyperopia 57% and entropy 27%. The refraction was performed using cycloplegic drops. Therefore, we will expect less myopia and more hyperopia. However, in the present study which examined the infants of Royan Institute, myopia was 6%, hyperopia 85% and emmetropia 9%. However, the refractive conditions of each person depend on their environmental and genetic factors [16]. Therefore, prevalence of refractive errors may be quite different in various races and communities [17]. Thus, it seems that ocular and visual data of below one year old infants must be accessible, but, unfortunately, no study is available on Iranian below one-year old infants. Therefore, it is necessary and unavoidable to conduct similar studies on Iranian and Tehran normal infants for more accurate comparison of the results obtained from the ART-exposed infants. Lack of normal control groups is of limitations of this study.

But studies conducted on Tehran and Dezful populations may be an estimation of from refractive conditions of some Iranian communities [17,18]. The results of the study on Tehran indicate 7.2% myopia and 6.5% hyperopia at age range of 5-15; whereas, in Dezful in age range of 7-15, myopia is 3.4% and hyperopia 16.6%. Percentage of people with astigmatism is 23.9% in Tehran and 18.7% in Dezful, which reached 38.6 in the present study. Other studies in other parts of the world often show less percentage of astigmatism. The study conducted by Axer et al also showed no difference in the percentage of astigmatism in the infants born by IVF and the infants fertilized naturally [3]. The study conducted by Wikstrand et al studied on visual function and ocular

morphology in the children fertilized using ICSI, indicates that no difference was observed between ICSI groups and the control group in levels of hyperopia, astigmatism, myopia, vision and convergence [19].

However, another study was conducted by Varghese et al on the relationship between birth weight, head circumference, fertilization age and birth time and refractive conditions [20]. The result of their study showed a significant correlation between physical parameters of growth and refractive conditions of the infants. The important recommendation of these researchers is screening in infants who do not have favorable growth parameters. Management of refractive errors in these infants can prevent much vision loss in their older age. Obviously one of the most important complications of refractive errors, especially astigmatism, is amblyopia.

The comparative study conducted by Ludwig et al on children who were fertilized using ICSI and normal control groups in terms of assessment of their vision and hearing, showed no significant difference between two groups in vision and hearing assessment [21]. The study of Basatemur et al on children from ICSI and IVF procedures and comparing them with normal growth parameters show lack of significant difference in these children compared with normal children at the same age, but their study and other similar studies emphasize that further studies are required for definite conclusion [22,23]. But the other ocular indicator examined in this study was the motility of these infants. In the conducted survey, by fixation conditions and doll's head maneuver of these infant respectively in 20.4% and 3.7% of cases indicated good results.

These results, compared with the results obtained in the study of Pedroso and Rotta, indicate the inappropriate conditions of the infants' reflexes resulting from assisted reproductive techniques [24]. Hirschberg test in infants suggests that there are 1/4 percent tropia in these infants. Exotropia and esotropia showed the same incidence frequency in the study. In other studies which investigated the population of Iran, the prevalence of strabismus in children was 0.8% [18]. Frequency of exotropia and esotropia in ART-exposed infants was the same, while the other studies did not show the same conditions of ocular aberrations distribution [18]. In the study of ocular aberrations in ART-exposed infants conducted by Anteby et al, the prevalence of strabismus in ART-exposed infants was announced about 4 percent. Another study conducted by Robaei et al on the population of Australian children suggests imbalance of frequency of EXO and ISO ocular aberrations [25]. They determined a significant correlation between the incidence of strabismus and prematurity.

Thus, it seems that ART-exposed infants may have more chances to get strabismus due to prematurity or low weight. But in the present study that not much prevalence was observed for this disorder (strabismus), its cause can be attributed to the lack of possibility of conducting accurate motility tests such as cover test. It seems inevitable due to the age conditions of infants. However,

some scientists have not essentially observed any difference in the ocular and visual conditions of ART-exposed infants and normal infants [3,19]. On the other hand, the specific conditions of these infants and evolutionary conditions of vision system cause some scientists to recommend visual screening of these infants [20,26,27]. These results evidently indicate the necessity of more extensive examination and follow-up of ART-exposed infants. These results suggest the possibility of refractive disorders, especially at older ages. These results also suggest the possibility of fixation and visual disorders in these infants. However, further studies will be needed for assurance. Obviously, consideration and comparison of these results in natural born babies without

assisted reproductive techniques could be very effective in informing infertility specialists, ophthalmologists, optometrists, pediatricians as well as their family. The initial report of refractive and fixation conditions of these infants may lead to the more attention of our various colleagues to the vision and ocular conditions of these infants.

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