Rīgas Stradiņa universitāte

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HETEROGENICITY OF CONGENITAL CATARACT AND ITS INFLUENCE ON PSEUDOPHAKIC EYE REFRACTION CHANGES

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ABBREVIATIONS

AL	axial length
CCUH	Children's Clinical University Hospital
BSS	balanced salt solution
ED	equatorial diameter
gauge cannula	standard scale cannula
HPO	Human Phenotype Ontology
IATS	*Infant Aphakia Treatment Study*
IC	inborn cataract
Infant	young child under one year of age
IOL	intraocular lense
IQR	interquartile range
MS	myopic shift
Newborn	infant in the first 28 days after birth
TR	target refraction
Ontology	the philosophical study of being
ORDO	the Orphanet Rare Disease Ontology
PREDA	the Register of Patients with Particular Disease and Congenital Anomalies
p-value < 0.05	was considered statistically significant
RSU	Rīga Stradiņš University
SD	standard deviation
SG	secondary glaucoma
SC	secondary cataract
CDPC (SPKC)	the Centre for Disease Prevention and Control of Latvia
TVL	*tunica vasculosa lentis*

INTRODUCTION

Venue of the Study

The Eye Clinic at Children's Clinical University Hospital, the Eye Clinic at Pauls Stradiņš Clinical University hospital, RSU Ophthalmology Department.

Topicality of the Study

Inborn cataract is one of most serious problems in paediatric ophthalmology. Untreated visually significant cataracts can cause lifetime blindness, reduced quality of life and increased socioeconomic costs to a child, family and society [9, 18, 17]. About 200,000 children in the world are blind due to untreated cataracts, complications of cataract surgeries, or other congenital anomalies related to cataract [9, 7, 32]. For the best possible vision development and prediction, both the time and type of inborn cataract treatment and the magnitude of the refractive error of the postoperative eye, its corrective capacity and the treatment of amblyopia play an important role [26, 27, 32].

In order to understand the inherited cataracts as a unique system, to compare the effects of the time and type of inborn cataract treatment on the size of the eye refraction error, types of visually significant inborn cataract, their interconnestions, size, development and dispersion of refraction error after cataract extraction and intra okular lens implantation surgery were investigated. Factors influencing eye refraction error after cataract extraction and IOL implantation surgery were formulated and compared. The study analysed the clinical data obtained in a defined region (Latvia) during a certain period (January 1, 2006–December 31, 2016).

Study Aims and Objectives

The aim of the study is to investigate and prove heterogenicity and factors of visually significant congenital cataract that influence eye refraction changes after cataract extraction with intraocular lens implantation.

The objectives of the study include:

- investigation of the characterising parameters of visually significant inborn cataract: morphology, time at cataract onset and laterality, and their interrelationship;
- definition of eye refraction changes after surgical correction of visually significant congenital cataract by intraocular lens implantation and proving its influencing factors;
- comparison of refraction changes in miopic shift in two different target refraction IOL implantation tactics: for emmetropy and hypermetropy groups;
- comparison of myopic shift in the eyes with different axial length during lens extraction and IOL implantation surgery;
- comparison of myopic schift in pseudophakic eyes with different individual IOL strength;
- working out methodological guidelines for examination and treatment of visually significant congenital cataracts at the Eye Clinic of Children's Clinical University hospital.

Hypotheses of the Study

Inborn cataract is a heterogenous unique system, its different characterising parameters – child's age at cataract onset, morphology and laterality – do not interact with each other. The chosen time and strategy for a cataract correction is based on individual cataract characteristics.

Axial length of an eyeball during cataract surgery affects pseudophakic refraction changes – its size and dispersion.

Different tactics of intraocular lens target refraction (emmetropic and hypermetropic IOL target refraction) do not affect myopic shift size, dispersion and amplitude. Intra ocular power of every eye, based on individul axial length and corneal curve at the time of a surgery might correlate with refraction changes.

Novelty of the Study

Statistically reliable evidence for the limit of eye length during surgical correction of congenital cataract was found in the study. The eyes of a length less than the obtained threshold after surgical correction with intraocular lens implantation will develop unpredictable and large myopic shift. The study found a statistically significant correlation between the individual IOL strength and the myopic shift of the eye. It has been proven to be statistically reliable that two different treatment tactics, when implanted in an intraocular lens, do not affect the size of myopic deviation of the refraction of the eye.

Practical Value of the Study and Implementation of the Study Results

For the first time the study of a visually significant inborn cataract was undertaken in Latvia. By changing the existent understanding of this disease, the tactic of treatment has been changed, and the algorithms for the examination and treatment of congenital cataract have been developed at the Eye Clinic in Children's Clinical University hospital. See Section Practical recommendations, No 1, No 2, No 3. Visually significant treated congenital cataract data basis in Children's Clinical University Hospital was developed.

1. MATERIAL AND METHODS

1.1. Sample Selection

Selected sample group involved 85 congenital cataract patients, aged 0–18 with 138 pseudophakic eyes. One of the three microsurgeons (GL, LR, JV) had performed lensectomies and IOL implantation operations to all the patients at Pauls Stradiņš Clinical University hospital in Riga, Latvia, at the time between January 1, 2006 and December 31, 2016. All patients were examined before the operation and followed up after the operation at Children's Clinical University hospital in Riga; it was performed by one of the ophthalmologists (the study author S.V.). Team of optometrists at Children's Clinical University hospital and vision pedagogues were involved into the work with patients. All patients underwent the operation according to the accepted indications, determining the visually significant amount and density of cataract as stated in the guidelines. If cataract was confirmed as visually significant, cataract operation was performed as soon as possible. In the study those patients were not included who along with congenital cataract were diagnosed with other significant ocular and systemic diseases. Prior to cataract surgical correction, the patients underwent profound eye examination, and an informative talk with the children's parents or caregivers was done. The Children's Clinical University Hospital's Ethics Review Board approved this research (see Attacment 1). All patients' parents or caregivers were informed about the child's disease, treatment, possible complications, and about the participation in the study, and the patients' data input into the study data base (see Attacment 2.). Patients' parents or caregivers signed the permission for surgical treatment and patients' data input into the study data base. In the study group all the treated visually significant congenital cataract cases were included within the above-mentioned period.

1.1.1. Study Sample Characteristics

The characteristics of the congenital cataract patients included in the study, the different treatment tactics and complication groups are presented in Table 1.1.

Table 1.1.

Distribution of eyes, patients and processes under study

Study cohort	**Classifications of inborn cataract**			**IK treat-ment tactic**	**IK complications**	
No of inborn cataract patients / eyes	Cataract onset time (eyes)	Morpholo gical (eyes)	Laterali ty: (eyes)	Emetro pic/ hypermetr opic target refraction (eyes)	With sec. glaucoma / without sec. glaucoma (eyes)	With sec. cataract / without sec.cat. (eyes)
138/85	66 congen. 30 infantiles 42 juveniles	23 total 27 lamellar 57 nuclear 22 post.polar 9 cortical	30 unilateral 108 bilateral	92/46	130/8	78/60

To characterise the eye with visually significant cataract heterogenity, the eyes of the study were divided according to different characterising factors of the congenital cataract: the time of cataract onset, morphology, and laterality.

The time of cataract onset was defined on anamnesis, case history and documentation in the patient's medical record. According to the time of cataract onset, all eyes in study sample were divided into congenital, infantile and juvenile cataracts. There were analysed 66 (47.83 %) congenital, 30 (21.74 %) infantile and 42 (30.43 %) juvenile inborn cataracts.

As to morphological classification, the operated inborn cataract eye distribution was as follows: 23 (16.67 %) total/difuse cataracts, 27 (19.57 %)

lamellar, 57 (41.30 %) nuclear cataracts, 22 (15.94 %) posterior polar cataracts and 9 (6.52 %) cortical cataracts. Cataract morphology in children from 3 years of age and in uncooperative children was determined by hand biomicroscope and operation microscope under general anaesthesia. During the examination, the photodocumentation of cataract was made. The acquired photographs were analysed both for clinical and study needs. The children who during cataract diagnostics time were over 3 years of age and those well cooperating with the treating physician and the researcher underwent routine biomicroscopy and, if possible, photodocumentation.

Laterality of congenital cataract was determined by the presence of cataract in one or both patient eyes. Unilateral cataract was seen in 30 (21.74 %) eyes, bilateral cataract in 108 (78.26 %) eyes. Bilateral cataracts were divided 75 (54.35 %) bilateral symmetrical and 33 (23.91 %) into bilateral asymmetrical cataracts.

After the onset of cataract, after determination of morphologic type and laterality, the decision was made on the type, time of cataract treatment and IOL target refraction. Inborn cataract in the selected study was treated with two different intraocular lens implantation tactics; two different implantable intraocular lens target refractions: emetropic and hypermetropic.

In the study 92 (66.66 %) emmetropic target refraction pseudophakic eyes and 46 (33.33 %) hypermetropic target refraction pseudophakic eyes were analysed. Since different treatment tactics were used considering the guidelines only on the earlier operated cataract then, by analysing congenital and infantile groups more in detail, the analysis was done for 51.6 % emmetropic congenital eyes, 8.4 % hypermetropic congenital eyes, 46.7 % emmetropic infantile eyes, 53.4 % hypermetropic eyes.

After the cataract surgical correction, two serious complications can result in after-effects of the treatment which in the future can affect eye refraction changes and vision development, such as secondary glaucoma (SG) and

secondary cataract (SC). Table 1.1. shows 8 (15.2 %) pseudophakic eyes with secondary glaucoma, 130 (84.4 %) pseudophakic eyes without SG, 60 (42.65 %) pseudophakic eyes with secondary cataracts and and 78 (57.35 %) pseudophakic eyes without SC.

Analysing the treated visually significant congenital cataract eyes, six groups were made based on the child's age at time of cataract extraction and intra ocular lens implantation. Since the greater changes in the eye growth occur in some of the first months, the operated eyes were divided nonlineary. Table 1.2. shows the child's age at time of primary surgical corection and number of eyes in every group.

Table 1.2.

Child's age at time of primary cataract extraction with intra ocular lens implantation

Age at the time of IOL Implantation (months)	1–6	7–12	13–24	25–48	49–84	85–216
Eyes/No. of patients	19/12	10/6	12/7	27/20	27/17	42/23

Theoretical basis of the child's age group during the primary surgical correction is described in the literature survey (see Section 1.9.2) [47, 53].

The second division – the division of the inborn cataract eyes, included in the study sample, into four groups formed based on eye axial length growth and four growth periods.

1.2. Time of Sample Group Observation

All the study cohort was observed, and the data was entered into the data analysis system. The minimum surveillance/observation length of time was 6 months, the maximum one – 120 months, mean observation time was 47.8 (SD = 37.21) months or 3.9 years. The patients' observation time is shown in the

histogram, Figure 1.1. For the choice of the observation time, an example from other scientists' experience was taken, which was summarised by *VanderVeen* in a table, the adapted version of which can be found in the literature survey [47].

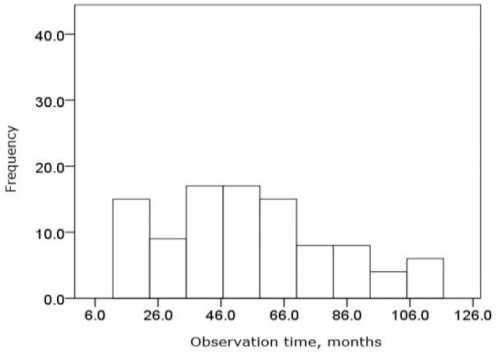


Figure 1.1. **Histogram of observation time of patients under study**

The study has included all visually significant operated congenital cataracts operated in Latvia within the last ten years. The children's age, when the cataract extraction operation and IOL implantations were performed was different; a similar observation time could not be provided for all patients under the study. In order to overcome it, myopic shift/per year was calculated for the patients in different inborn cataract surgery age groups. Medium, positive, and statistically significant correlation was acquired between the children' age groups during IC surgery and myopic shift amount per year ($rs = 0.062$; $p = 0.001$), which confirmed that the medium observation time can substitute one certain observation length and statistically significantly depict the outcomes.

1.3. Measurements of Eye Axial Length and IOL Individual Power

Prior to cataract extraction operation and IOL implantation, the eye axial length of the patients was measured by ultrasonographic A Scan method. 10 automatic eye anterior-posterior axis measurements were fixed, and the medium

eye axial length size was calculated. In children by the age of 3 years and those who did not cooperate the measurements were done under general anaesthesia. The eye axial length was calculated using the ultrosonographic A Scan method, and keratometry data were acquaired using the standard or hand keratometer. IOL calculations of older children and eye axial length measurements were done by IOL Master programme. For the calculation of IOL power, SRKT and Holliday I IOL calculation formulae were applied.

1.3.1. Periods of Eye Growth and Axial Length Changes in Them. Distribution of Eyes of Patients after Performed Primary Surgeries at Different Periods of Eye Growth

The growth of an eyeball can be divided into three periods [10; 24]. In the fast postnatal growth phase, in the first 18 months after the birth of the child, the eye axial length increases by 4.3 mm (on average from 16 mm till 20.3 mm), in the infantile growth phase, from 2 to 5 years of age, the axial length increase is on average 1.1 mm, in the slow juvenile phase, from 5 to 13 years of age, the increase of the axial length is 1.3 mm (Figure 1.2).

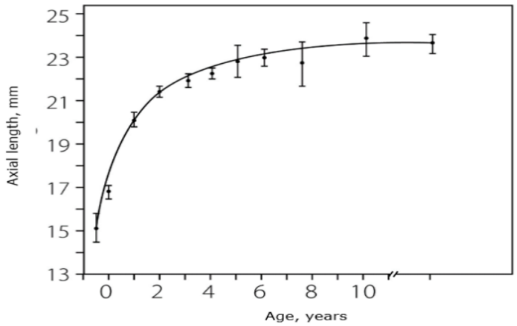


Figure 1.2. **Increase of axial length along with the growth of a child**

Since the axial length of an eyeball directly affects the refraction of the eye comparing the changes in eye refraction after cataract extraction surgical

correction with IOL implantation, different periods of the growth of the eye and the age of the child were considered; separation of the eyes of the patients included in the study after primary surgical correction of the inborn cataracts in different stages of the growth of the eye. Four groups were obtained with no significant differences (Figure 1.3) in the number of eyes (p = 0.13).

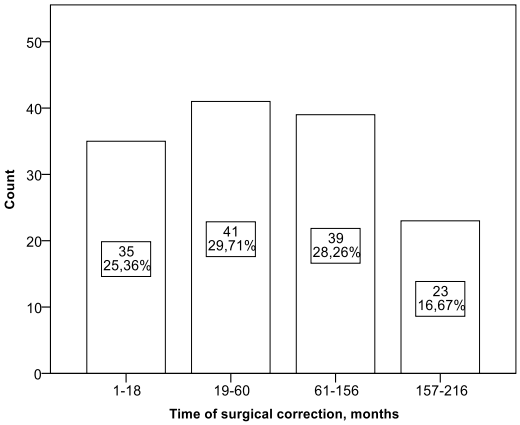


Figure 1.3. **Number of eyes in different stages of the growth of the eye**

1.4. Intraocular Lens Power Target and Two IOL Implantation Tactics

Based on the two different intraocular lens implantation tactics (Table 1.3) – two different implantable intraocular lens target refractions – when starting the study, one retrospective subgroup in the study selection was formed – congenital cataracts with emmetropic target refraction, operated on between 2006 and 2010, and one prospective subgroup – congenital cataracts with hypermetropic target refraction, operated on bewteen 2010 and 2016. At the same time, dividing all patients under study into groups according to cataract onset, in the patient selection there were developed 19 emmetropic congenital

IOL target refraction eyes, and 29 hypermetropic congenital IOL TR eyes, 17 emmetropic infantile TR eyes and 18 hypermetropic infantile TR eyes. All (42) juvenile congenital cataract eyes were with emmetropic target refraction. Theoretical substantiation for the choice of target refraction has been decribed in the literature survey (See Table 1.3.).

Table 1.3.

Intraocular lens target power for IOL implantation at different children ages

Age at the time of cataract extraction and IOL implantation	< 12 months	1–2 years	3–4 years	5–6 years	7–8 years
IOL target refraction	+ 10–+7 D	+6 D	+4 D	+3 D	+1.5 D

Adapted from Wilson, Trivedi, Suresh "Paediatric Cataract surgery"; 2005 [53].

1.4.1. Distribution of Eyes of Patients According to Two Treatment Tactics

Analysing two tactics of IOL implantation – emmetropic and hypermetropic intraocular lens refraction – in relation to the age of cataract onset groups, two similar groups developed in congenital and infantile groups which, as to the number of implanted lenses, practically did not differ between themselves (Figure 1.4). We can exclude juvenile group from this comparison because in this group target refration in all eyes was emmetropic.

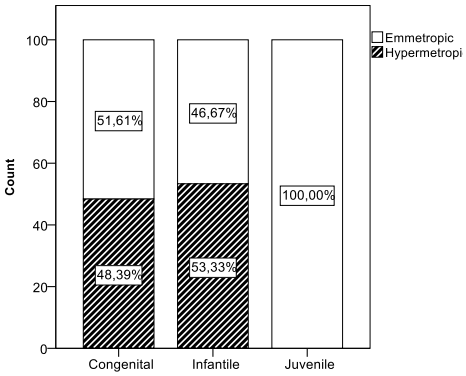


Figure 1.4. **Distribution of emmetropic and hypermetropic target refraction tactics of IOL implantations into congenital and infantile IC cataract groups**

1.4.2. Individual Power of Implanted Intraocular Lens of Inborn Cataract Pseudophakic Eyes

In each congenital cataract eye, an individual IOL power is measured. In the study, the individual IOL powers ranged from 10 D to 36 D. In the congenital group the minimum of implanted IOL power was 11 dioptries (D), the maximum – 40 D, on average it made 28.03 D. In the infantile group, on average, the implanted intraocular lens power was 25.12 D, in the juvenile group – 24.45 D.

1.4.3. Measuring Postoperative Refraction Error

Of all the eyes included in the study, refraction error was meassured for two weeks after primary surgical correction with intra ocular implantation in full cycloplegia by *Sol. Cyclopentolate hydrochloride 0.5 % or 1 %* - 1 drop in each eye two times every 5 minutes, after dropping the wait time was 30–40 minutes. Measurements were done by retinoscope and handheld or standard autorefractometer.

1.5. Pseudophakic Eye Refraction Changes or Myopic Shift

Myopic shift or refraction changes in myopic direction after primary cataract extraction and intraocular lens implantation surgery was defined and calculated like a refraction error's spheric equivalent difference during the last examination time and in the first examination – 2 weeks after lensectomy and intraocular lens implantation.

1.6. Assessment of Vision Acuity and Amblyopia Treatment

The best corrected vision acuity in children up to 3 years of age was determined by preferential looking tests, using *Cardiff Acuity Cards*. In older children the distant vision was measured by E letter test, Figure table test, digital table test in 5 m distance and Lea test or E letter test in the near (40 cm). By the acquired vision acuity results during the last postoperative examination, the vision was estimated as very good (5) – Visus 20/25–20/20, good (4) – Visus 20/40–20/30, moderate (3) – Visus 20/60–20/50, low (2) – Visus 20/100–20/200 and very low (1) – up to 20/200. Combining the first two groups, one group was made in which the vision acuity was estimated as good. In the same way, by combining the two last groups, marking all vision acquities that were in this group as being low. As a result, three vision assessment groups were formed for the comparison: good, moderate and low vision groups.

1.7. Statistical Analysis

In order to analyse the patients' demographic and clinical parameters, descriptive statistical methods were used. Normally divided quantitative parameters were described as the mean (M) and standard deviation (SD), in the opposite case there were used median (Me) and standard quartiles dispersion amplitude. Qualitative variables were expressed as number (N) and percentage

ratio (%). Two groups' quantitative data were analysed by t-test or Mann-Whitney test, while three and more groups were analysed by using dispersion analysis (ANOVA) or Kruskal-Wallis test. Data distribution dispersion analysis was done by Levene test. Spearman (rs) correlation coefficient analysis was used to analyse relationships between the continuous variables. Linear regression analysis was used for the assessment of quantitative influence. Qualitative data were analysed using Pearson chi square or Fisher precise test, according to the conditions of use. Two-sided p-value < 0.05 was considered statistically significant. Statistical analysis was done using IBM SPSS programme (Windows version 23, IBM Corp., Somers, NY, USA).

2. RESULTS

2.1. Characterising Parameters of Inborn Cataract – Time of Cataract Onset, Morphology, Laterality and Their Interrelationship

2.1.1. Interrelationship of Inborn Cataract Onset Time and Morphological Type

Studying the interrelationship of inborn cataract time of onset and the morphological type, morphology of IC within different time of onset groups was analysed. The data have been represented in Figure 2.1.

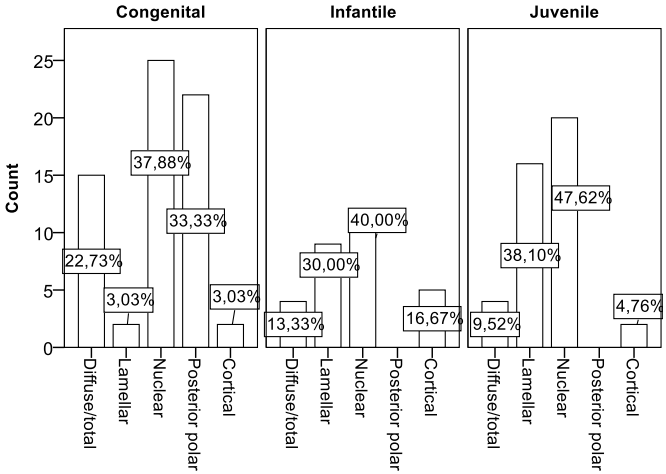


Figure 2.1. **Distribution of inborn cataracts of different onset time by IC morphological type**

In the congenital group with 66 pseudophakic eyes, the most commonly diagnosed were diffuse/total – 15 (22.73 %), nuclear – 25 (37.88 %) and posterior polar – 22 (33.33 %) cataracts. Nuclear cataracts were most commonly found also in the infantile group –12 (40.00 %) and juvenile group – 20 (47.62 %). In

the infantile group there were 30 pseudophakic eyes in total, in the juvenile group – 42 pseudophakic eyes. In the juvenile group there were also quite commonly found lamellar cataracts – 16 (38.10 %). The least common ones were cortical congenital cataracts; there were 2 (3.03 %) in the congenital group, in the infantile group – 5 (16.67 %), in the juvenile group – 2 (4.76 %).

Comparing different morphological cataract type proportions in cataract onset groups, statistically significant proportions were found in several groups. For instance, posterior polar cataract amount proportion statistically significantly differed both in the congenital and infantile groups where Z proportion between congenital and infantile group was 3.6018 ($p < 0.001$), and in the congenital and juvenile groups where Z proportion was 4.2 ($p < 0.001$). Comparing the cortical cataract amount in the congenital and infantile groups, Z proportion was – 2.4 ($p = 0.02$), which shows a statistically significant difference. In the comparisons of other groups, the differences were not so significant, though they show that in any of IC onset time groups any morphological cataract version is possible. For instance, nuclear cataract amount in the congenital and infantile groups did not statistically significantly differ – Z proportion was – 0.2 ($p = 0.84$). However, such data comparison gives evidence that cataract morphology at different onset times of cataract may be very different.

2.1.2. Interrelationship of Inborn Cataract Onset Time and Laterality

Studying inborn cataract laterality in different cataract onset time groups, the following results were acquired, shown in Figure 2.2.

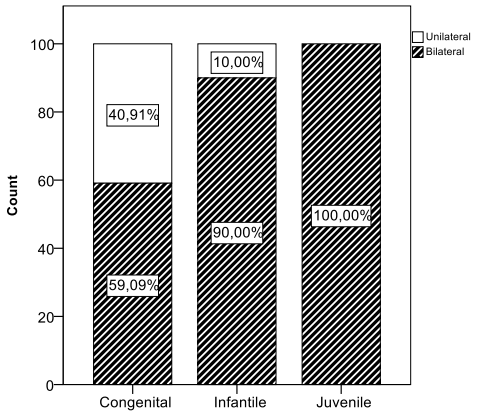


Figure 2.2. **Inborn cataract distribution by laterality in cataract onset time groups**

In the congenital group, there were diagnosed unilateral (40.91 %), and bilateral (59.09 %) cataracts. In the infantile group, there were fewer unilateral cataracts, only three (10 %) unilateral cataract eyes were diagnosed. In the juvenile group there were only bilateral cataract eyes (100 %). Comparing unilateral cataract amount in the congenital and infantile groups, Z proportion was 3.02 ($p = 0.002$), which demonstrates a statistically significant difference. Since no unilateral cataract was diagnosed in the juvenile group, here Z proportion test demonstrates a statistically significant difference as well.

2.1.3. Interrelationship of Inborn Cataract Morphological Type and Laterality

Studying different morphological type laterality, one can see that diffuse/total cataracts of 91.30 % cases are bilateral; lamellar cataracts in our study selection in 100 % were bilateral, 84.21 % of nuclear cataracts were bilateral. Posterior polar cataracts in 68.18 % cases were unilateral, cortical cataracts in 44 % cases were unilateral (see Figure 2.3).

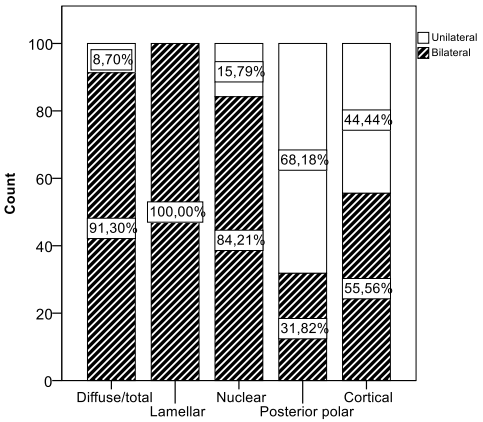


Figure 2.3. **Distribution of inborn cataract morphologic types by laterality**

Comparing the unilateral cataract amount in different morphological variants of cataracts, there were found several statistically significant proportional differences. For instance, comparing diffuse/total and posterior polar cataracts, Z proportion in relationship to unilateral and bilateral cataract amount in these groups was – 2.33 (p = 0.02), which shows a statistically significant difference. In the same way, statistically significant will be Z proportion difference between the total diffuse and cortical cataract lateralities. However, comparing the total/diffuse and nuclear cataract lateralities, Z proportion was – 0.8339 (p = 0.40), which does not show a statistically significant difference.

2.2. Inborn Cataract Treatment Time, Its Relationship to IC Classifications and Treatment Complications

2.2.1. Inborn Cataract Primary Surgical Correction Time for Different IC Morphological Types

Investigating and analysing the morphological structure of inborn cataracts, and considering the cataract onset time and laterality, the decision was

taken on the surgical correction time for visually significant cataract. Analysing the child's age during the cataract surgery and variability of cataract morphology, the data were acquired, shown in Figure 2.4.

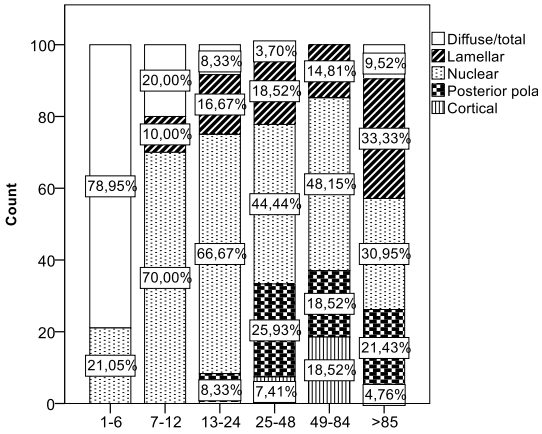


Figure 2.4. **Distribution of operated IC at different ages by the morphological type of cataract**

At an early age, in children from 1 to 6 months, only diffuse/total and nuclear cataracts were operated. With the increase in the patients' age, the number of total/diffuse operated cataracts decreased, while other congenital morphological types of operated cataracts increased. Posterior polar cataracts in our selection were operated after 12 months of age. At the age from 4 to 8 years not a single diffuse/total cataract was operated, but at the age after 8 years all encountered morphological cataract types got operated (see Figure 2.4).

2.2.2. Primary Surgical Correction Time of Congenital Cataracts in Different Cataract Laterality Groups

The child's age of unilateral and bilateral congenital inborn cataracts during primary surgical correction time is shown in Figure 2.5.

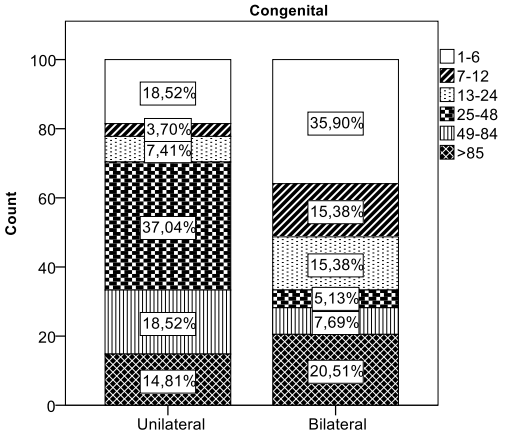


Figure 2.5. **Primary operative treatment time of unilateral and bilateral congenital cataracts**

Bilateral congenital cataracts were operated on children at all ages. Congenital unilateral cataracts were also operated on children at all ages. Comparing the children's age during the primary surgical correction time, there were found statistically significant proportional differences by Z proportion test in one children's age group – from 25 months to 48 months, where Z proportion was 3.30 ($p < 0.001$). In other groups statistically significant proportional differences were not observed. However, the different primary surgical time also points at the variety of congenital cataracts.

2.2.3. Secondary Glaucoma and Its Incidence at Different Inborn Cataract Surgery Time Correspondingly to the Periods of the Eye Growth

To analyse the incidence of secondary glaucoma, the child's age during the primary surgical correction time and IOL implantation time in relation to the eye growth phase were chosen. Analysing the incidence of secondary glaucoma at different periods of the eye growth the data shown in Figure 2.6 were acquaired.

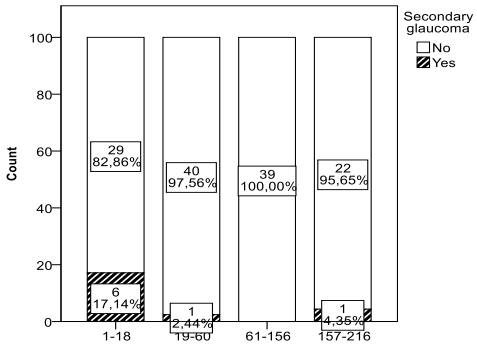


Figure 2.6. **Incidence of secondary glaucoma in pseudophakic inborn cataract eyes, operated at different periods of eye growth**

Analysing the incidence of secondary glaucoma in all study selection, SG was diagnosed in 8 (15.2 %) eyes. Comparing the periods of eye growth, most commonly secondary glaucoma was seen in the eyes which had been operated in the postnatal fast period of the eye growth – at the time till the child reaching 18 months (77.8 % of all secondary glaucoma cases). Comparing proportions of secondary glaucoma at the fast eye growth period and in the slow infantile eye growth period, statistically significant difference was found (Z proportion = 2.66, p = 0.007), comparing it also to juvenile slow eye growth period (Z proportion = 2.03, p = 0.04), and the period when the eye stops growing (Z proportion = 2.14, p = 0.03); the incidence of secondary glaucoma proportional differences was statistically significant.

2.2.4. Secondary Cataract and Its Incidence at Different Periods of Inborn Cataract Surgeries Correspondingly to Different Operation Types used

To analyse the incidence of secondary cataract, periods of the child's age were chosen when for the inborn cataract surgical correction different operative

techniques were used, which are described more in detail in the materials and methods.

Analysing the pseudophakic eyes in the study selection, secondary cataract (secondary cataract and/or reproliferations of optic axis) was diagnosed at all inborn cataract treatment periods. In the total selection, the secondary cataract was diagnosed in 58 (42.65 %) eyes. As seen in Figure 2.7, in the group where the eye operation was done in the period when the child was between 1 and 24 months, performing the cataract extraction, the posterior capsulorrhexis and anterior vitrectomy, the secondary cataract was diagnosed in 17 eyes (41.46 %). In the period between 24 months of age and 84 months of age, when the cataract extraction and posterior capsulorrhexis were done, in the postoperative period the secondary cataract was diagnosed in 26 eyes (48.1 %), at the time after 84 months of age, when only the cataract extraction was done, the secondary cataract was diagnosed in 13 eyes (32.5 %) (see Figure 2.7).

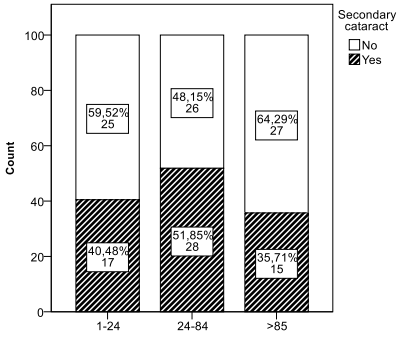


Figure 2.7. **Incidence of secondary cataract in pseudophakic IC eyes, operated by different methods at different periods of child's age**

Comparing proportions of secondary cataract in children, operated by different methods and at different periods of age, no statistically significant proportion was found ($p = 0.5$, analysing the 1st and the 2nd group; $p = 0.4$, analysing the 1st and the 3rd group; $p = 0.13$, analysing the 2nd and the 3rd group).

Also, in Pearson chi square statistical test analysis between different operation types, and different children' age groups, and the incidence of secondary cataract no statistically significant difference was found ($p = 0.16$).

2.3. Refraction Changes in Pseudophakic Eyes – Myopic Shift and Its Influential Factors

Surgical correction of cataract extraction with the intraocular lens implantation breaks up the natural emmetropisation of eye refraction. Since the eyeball in infancy is growing, with its axial length increasing, eye refraction will change into myopic direction. In the study significant postoperative eye refraction change – myopic shifts – amount was investigated and its relationship to the child' age at surgical correction time; different periods of eye growth; IC morphological types; IC laterality; different IC implantation techniques; each eye's implanted idividual IOL power and postoperative complications.

2.3.1. Comparison of Myopic Shift in Various Inborn Cataract Surgeries at Different Children's Age Groups and Different Periods of Eye Growth

Differences of myopic shift depending on lensectomy and IOL lens implantation time are shown in Figure 2.8 a and b.

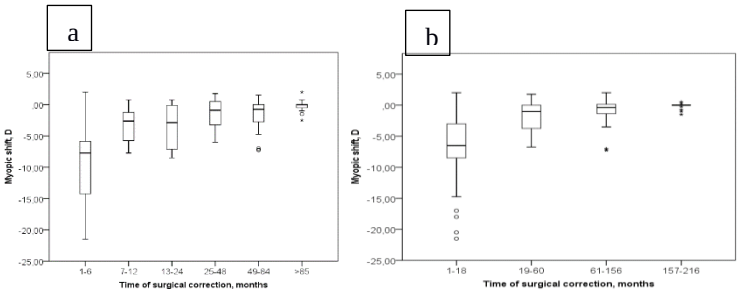


Figure 2.8 a and b. **Comparison of myopic shift parameters in IC surgeries (a) in the children's age groups and (b) in various periods of eye growth**

Comparing MS of the operated IC eyes during the maximum observation time, operated at different children's age periods, it was observed that in the eyes which had been operated on earlier (from 1 to 6 months of age), MS showed a statistically greater significance rather than at the later surgical correction time periods ($p < 0.05$). As seen in Figure 2.8 a, myopic shifts in median group, operated on from 1 to 6 months was –7.75 D, in the next cataract surgery children's age group (7–12 months), the median decreased three times, reaching –2.62 D. Comparing the second and the third group, involving the eyes operated on up to 12 months of age, the development of myopic shifts in these groups practically did not change (MS median = –2.87 D). If congenital cataracts are operated on at the children's age from 25 months to 18 years, then myopic shift median is approaching a zero.

Comparing MS dispersion at different periods of eye growth, shown in Figure 2.8 a and 2.9 a, it was observed that the greatest dispersion amplitude was seen in the fast eye growth phase in the period from 1 to 18 months (23.5 D), while in the period when it stops growing (157–216 months), MS dispersion amplitude was 2 D. Analysing myopic shift dispersion in various eye growth phases, MS dispersion in the postnatal fast eye growth phase statistically significantly differed from the rest of the eye growth phases – infantile and juvenile slow growth phases and the period when the eye growth does not occur

(Levene test, $p < 0.05$). In both slow eye growth phases, the operated IC myopic shift did not statistically differ ($p > 0.05$). Comparing MS which operated in the slow eye growth phases (19–60 months and 61–156 months), with the time when the eye stops growing (157–216 months), statistically significant differences were acquired between MS 2nd and 4th group, and the 3rd and the 4th group (Levene test, $p < 0.01$). Myopic shift dispersions in different eye growth periods are shown in Figure 2.9 b.

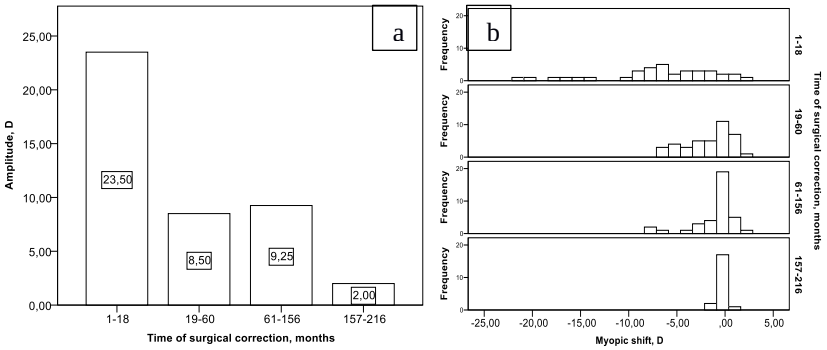


Figure 2.9 a and b. **Myopic shifts (a) comparison of amplitudes and (b) histogram in different eye groth phases**

2.3.2. Correlation of Myopic Shift with Axial Length of Inborn Cataract Eye during Cataract Extraction and IOL Implantation Time

With the growth of the child, the eye axial length is markedly expanding within the first two years of life. Comparing myopic shift parameter during the maximal observation time and the eye axial length during cataract extraction and IOL implantation time, a statistically significant correlation was found (see Figure 2.10).

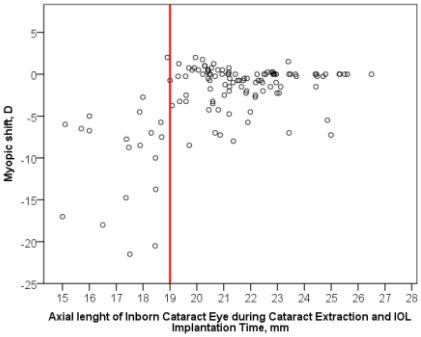


Figure 2.10. **Correlation of myopic shift and the eye axial length during the primary surgical correction**

In the analysis of Spearman correlation coefficient between the eye axial length and myopic shift, there was found medium, positive and statistically significant correlation rs = 0.30; p = 0.01).

Drawing MS standard deviations and dispersions in different eyeball length cases during the surgical cataract correction, a relationship was noticed, showing that MS in inborn cataract eye group, whose eye axial length was less than 19 mm, was greater and differed from IC eyes, whose axial length was 19 mm and higher.

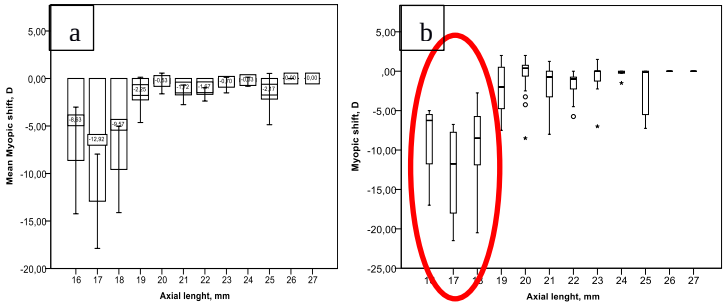


Figure 2.11 a and b. **Myopic shifts (a) standard deviations, median and (b) dispersion in relationship to inborn cataract eye axial length**

Comparing myopic shift parameter in the eyes which are < 19 mm, and the eyes which are ≥19 mm, results shown in Figure 2.12 were acquired.

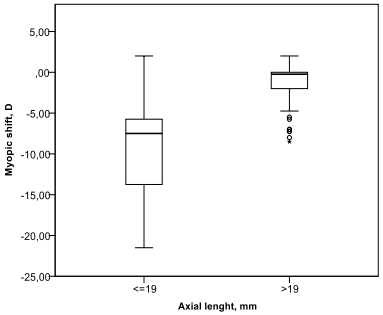


Figure 2.12. **Comparison of amount of myopic shift in eyes with axial length < 19 mm and ≥ 19 mm**

For the eyes with axial length of < 19 mm, myopic shift median was −7.5 D [−5.37 – −14.25], but the eyes with axial length ≥ 19 mm, myopic shift median was –0.25 D [0 – –2.00 D]. Checking myopic shift dispersions of the eye groups the axial length of which was < 19 mm and ≥ 19 mm, it was found that they differ statistically significantly (Levene test, $p < 0.001$).

2.3.3. Comparison of MS Parameters in Groups of Cataract Onset Time and Cataract Morphological Classification

Myopic shift in pseudophakic eyes statistically significantly differed from cataract onset time and morphology groups (see Figure 2.13 a and b).

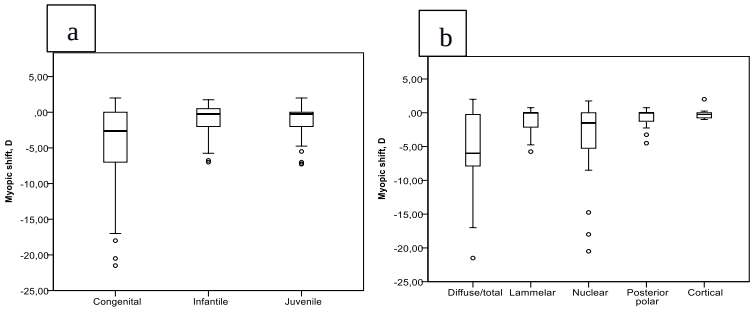


Figure 2.13 a and b. **Comparison of myopic shift in (a) cataract onset time classification groups and (b) cataract morphology groups**

In the congenital group, 75 % myopic shift range was from + 2.0 D to – 7.75 D, 25 % of the eye MS range in the congenital group statistically significantly differed from the MS range in the infantile and juvenile group (ANOVA, $p < 0.05$). In the infantile and juvenile groups, the MS parameters were much lesser (see Figure 2.13 a). Comparing morphologic congenital cataract groups (see Figure 2.13 b), the MS parameter in total/diffuse cataract morphology group was markedly higher and statistically significantly differed from the MS in the lamellar, nuclear and posterior polar morphology group ($p < 0.05$). Parameters of myopic shift, in its turn, in the lamellar, nuclear and posterior morphologic group did not statistically significantly differ between themselves ($p > 0.05$).

2.3.4. Comparison of Amount of Myopic Shift in Unilateral and Bilateral Congenital Cataracts

The size of myopic shift on operated unilateral and bilateral congenital cataracts in the eyes is shown in Figure 2.14. Since, by dividing unilataral and

bilateral congenital cataracts into groups corresponding to the child's age during surgery, the number of unilateral cataracts in several groups was insignificant, and myopic shift dispersions in them were minimal, operated unilateral and bilateral IC eye myopic shifts were compared at an early surgery age – aged between 1 and 6 months, and children whose IC surgical correction was performed at a later period.

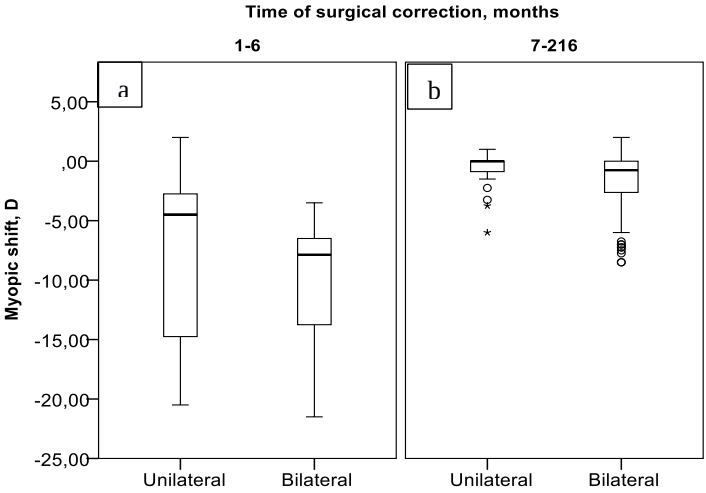


Figure 2.14. **Comparison of MS in unilateral and bilateral congenital cataracts on whom surgical correction was done (a) at an early age (1–6 months) and (b) at the age from 6 months to 18 years**

The difference which had developed between the myopic shift in unilateral and bilateral operated inborn cataracts in the eyes in different IC surgical correction age groups was not statistically significant ($p > 0.05$). At an early age primary surgery group (the age from 1 to 6 months), median in bilateral IC cases was 1.7 times higher than in unilateral IC cases, yet the difference was not statistically significant.

2.4. Comparison of Amount of Myopic Shifts in Operated Inborn Cataract Eyes, Using Different Tactics of IOL Implantation

Analysing the operated IC eyes, on which two different IOL implantation tactics had been used for IOL implantation (emmetropic and hypermetropic IOL implantation target refraction) in the cataract onset time groups, no statistically significant ($p > 0.05$) difference of the amount of myopic shift was found during the maximum observation time (see Figure 2.15).

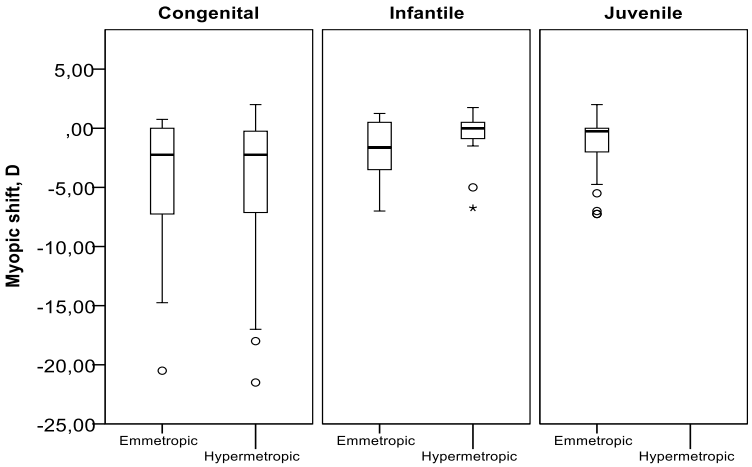


Figure 2.15. **Comparison of myopic shift after emmetropic and hypermetropic IOL target refraction implantation in pseudophakic eyes in cataract onset time classification groups**

Comparing myopic shifts in different IOL implantation tactics groups in the form of histogram, the following Figures and a comparison was obtained (see Figure 2.16 a and b).

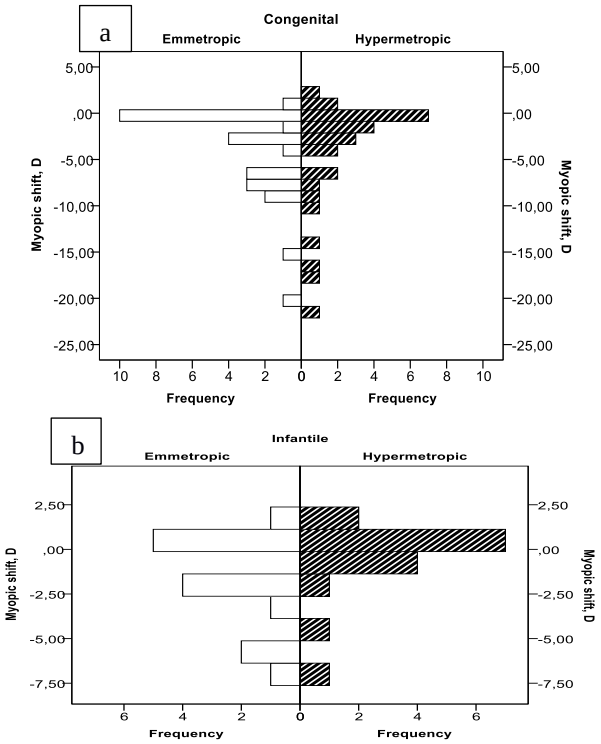


Figure 2.16 a and b. **Comparison of histogram of myopic shift parameter in congenital (a) and infantile (b) congenital cataracts, treated by two different IOL implantation tactics**

Myopic shift of two congenital IC treatment tactics (emmetropic and hypermetropic IOL target refractions) groups during the maximum observation time did not statistically significantly differ (Mann-Whitney test, $p = 0.64$), similarly, no difference was found also in the infantile group (Mann-Whitney test, $p = 0.25$).

2.5. Correlation of Myopic Shift with Individual IOL Power of Pseudophakic Inborn Cataract Eyes

Comparing the size of myopic shift and individual eye IOL power at various ages on operated pseudophakic eyes, statistically significant differences were noticed (Figure 2.17).

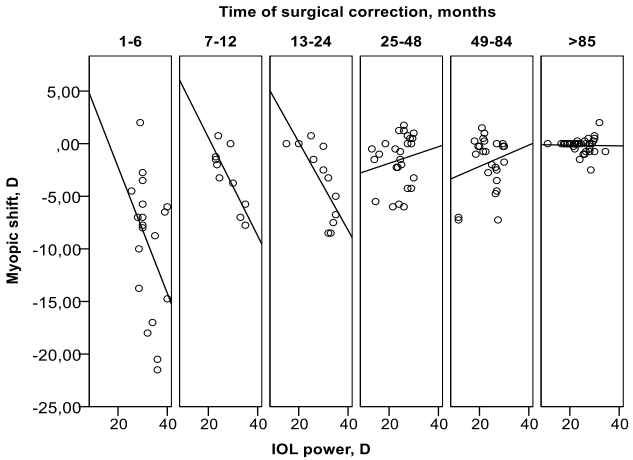


Figure 2.17. **Comparison of myopic shift in eyes with different IOL power in children's age groups during IC surgery**

In the pseudophakic eye group, in which the operation was performed on children from 1 to 6 months of age, a medium correlation between MS and intraocular lens power (rs = – 0.38) was found to be negative; however, it could be considered only a tendency because it did not have statistical significance (p = 0.10). By linear regression analysis, it was found that with IOL power increase by 1 D, myopic shift increased on average by 0.61 D (p = 0.01). In the group of inborn cataracts operated at child's age from 7 to 12 months, the negative, close and statistically significant correlation was found between MS and IOL power (rs = –0.74; p = 0.01). In the linear regression analysis, it was found out that by IOL power increase by 1 D, MS increased on average by 0.46 D (p = 0.01). In the group where the operative therapy was introduced to the children from 13 to

24 months, a negative, close and statistically significant correlation was found between MS and IOL power (rs = – 0.82; p = 0.001). Linear regression analysis showed that with IOL power increase by 1 D, MS increased on average by 0.41 D (p < 0.001). Negative correlation between myopic shift and IOL power was seen in the eyes operated up to 24 months of age, but in the eyes operated after 24 months of age, no statistically significant correlation was observed between these parameters (p > 0.05).

2.6. Comparison of Myopic Shift of Psedophakic Inborn Cataract Eyes to Different Postoperative Complications – Secondary Glaucoma and Secondary Cataract

Analysing the complications, after effects of primary surgical corrections of congenital cataracts, myopic shifts of the patients' eyes were compared during the maximum observation time – the eyes with secondary glaucoma and without it, and the eyes with secondary cataract and without it operated in the first six monthes and the rest of time (see Figure 2.18 a and b).

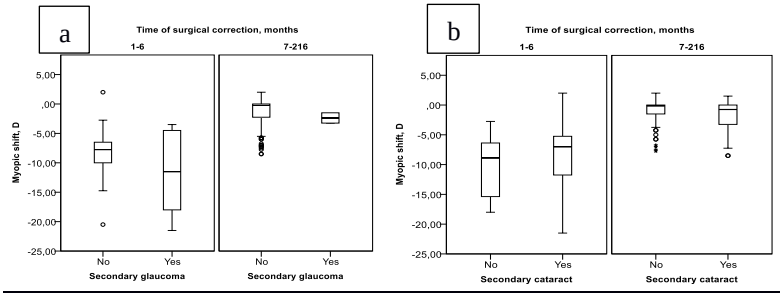


Figure 2.18 a and b. **Comparison of myopic shifts in operated IC eyes (a) with secondary glaucoma and without it and (b) with secondary cataract and without it operated in the first six monthes(1-6) and at other time (7–216 months)**

At the first 6 monthes operated IC eyes with secondary glaucoma and without it, no statistically significant myopic shifts' median difference was found (Mann-Whitney test, $p = 0.01$); however, visually (see Figure 2.18 a) one could notice the tendency that in the case of secondary glaucoma, myopic shift can be greater. Checking the difference of dispersion in eyes with secondary glaucoma and without it operated at the first six months, there was found a statistically significant difference (Levene test, $p = 0.02$). In secondary glaucoma patients the dispersions were greater rather than in patients without secondary glaucoma (see Figure 2.18 a).

In the first six months operated IC eyes with secondary cataract and without it no statistically significant myopic shift's median difference (Mann-Whitney test, $p = 0.70$) was found. Checking the dispersion difference of operated eyes with secondary cataract and without it, no statistically significant differences were found (Levene test, $p = 0.45$) (see Figure 2.18 b).

2.7. Effect of Amount of Myopic Shift of Pseudofakic Eyes on Development of a Child's Vision

The chief aim of congenital cataract treatment is the development of a child' vision. Dividing myopic shift parameters in three groups and comparing the assessment parameter of maximum acquired vision in each of these groups, the results were acquired, shown in Figure 2.19 and Table 2.1.

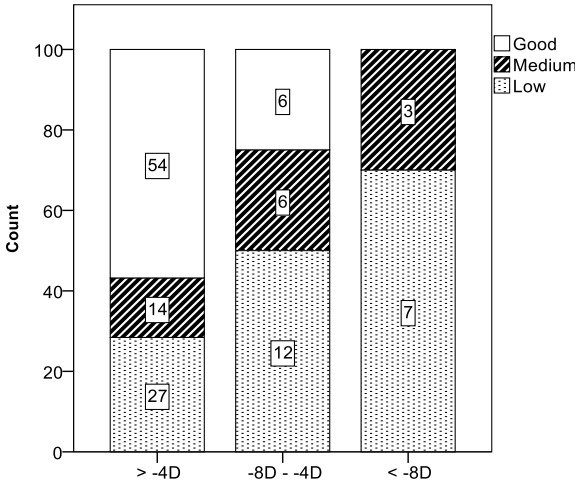


Figure 2.19. **Correlation of myopic shift of operated IC eye refraction in relation to assessment of eyesight**

Table 2.1.

Effect of myopic shift of pseudofakic eyes on development of vision

Myopic shift (D)	Low vision %	Medium vision %	Good vision %
> –4.0 D	28	17	55
From –4.0 D to –8.0 D	50	25	25
< –8.0 D	70	30	

The acquired results show – if the eye myopic shift after congenital cataract correction is up to –4 D, then 55 % of eyesight is considered as good, 17% – moderate, but 28 % – low. If the eye myopic shift parameter is from –4 D to –8 D, only 25 % of the eyes will acquire good eyesight. If myopic shift exceeds –8 D, neither of the eyes under the study could be considered as good.

3. DISCUSSION

The objective of the study was to investigate congenital cataract as a unique, united, heterogenous nosological unit, to summarise and visually show congenital cataract classes and the effect of their interrelations.

Since cataract is the opacity of lens, and the eye lens is one of the components of the eye optical system, it means that either treated or untreated, it will always affect the refraction error and create changes of refraction error. Cataracts at infacy and at a toddler's age differ from cataracts in adulthood and in children at the age of 7 years, because the effect of cataract interferes as a result of a condition or illness, or it functions simultaneously with the development of the system of eye vision [9; 19].

The research analyses surgically treated congenital cataract-induced refraction changes after cataract extraction and intraocular lens transplantation operations during a child's growth period and the growth of an eyeball. Both workload and benefit mean the wish to consider all factors which characterise congenital cataract and its treatment, all factors to be considered in the daily clinical practice when treating an infant and a child with congenital cataract.

It was analysed how error changes of eye refraction after congenital cataract surgical correction by IOL implantation affect different types of IC, a child's age and the eye axial length during the primary surgical correction, different 42ontrover tactics, individual intraocular lens power and most common postoperative complications.

Heterogenicity of congenital cataracts has been shown by simultaneousity of different IC classifications. Each single congenital cataract can develop at different times, which has been depicted by the classification of cataract onset. Simultaneously, it can take different morphological types, as well as it may be developed only in one eye, or in both eyes of a child. This has been represented

in Table 1.1 as the characterisation of the material and its outcome. Different inborn cataract types fit into and supplement each other.

Inborn cataracts can start at any age of a child. According to cataract onset time, IC is classified as congenital – opacity developing while in uterus and is seen just after the birth, infantile – lens opacity develops and is seen within the first two years of life, and juvenile – opacity in the eye lens is developing after two years of life. Such a classification can be found in Wilson et al. book "Paediatric Cataract Surgery" [54].

When analysing lens opacity in different morphological structures of a child's eyes, cataract can be classified by the name of lens morphological structure. For instance, the first to become opaque is the lens embryonic nucleus, followed by opacity of foetal nucleus and then entire eye lens. In a different case, eye lens nucleus can remain 43ontroversi while the lens cortex around it gets opaque, forming different type and pattern cataract. One can commonly see opacities in the posterior eye lens capsule, or in its neighbourhood. Morphological type of congenital cataract will influence a patient's surgical treatment time differently, as well as the type and incidence of complications, nuances of the operation techniques, and vision prognosis during a child's growth [8; 16; 26; 36]. In the current study, morphologic structure of cataract has been determined using biomicroscope or hand biomicroscope and/or operation microscope. In the randomised multicentre prospective study "Infant Aphakia Treatment Study" (IATS), 83 congenital cataract structure videos during cataract extraction operation were analysed by three experts on congenital cataract treatment, later deciding on the type of cataract morphology, applying a score sheet to record the lens layer or configuration of the opacity [52]. The classification of congenital cataract by morphological distribution of opacity allows classifying the cataract, to determine its treatment tactics, the time and possible prognosis [1; 8]. Phenotypic cataract heterogenicity in congenital cataract cases is commonly found. Within a pedigree, one can observe different

cataract morphological varieties. It will not be so simple that one gene mutation will define one type phenotypic change; a different gene can modify a causative gene mutation. Morphological differences can be either intraocular (asymmetric cataract in bilateral cataract cases), or intrafamiliar (different type and intensity cataracts within one pedigree patient [1; 27].

Congenital cataract can be in one eye or in both. Comparing treatment outcomes, vision ability in the eyes with bilateral or unilateral cataracts in children with a unilateral cataract, one could identify a poorer vision development; quite often it was observed to have moderate or severe one eye weakness [4]. Etiology of unilateral and bilateral cataract is different. Hereditary disease is considered to be the cause of congenital cataract in half of bilateral congenital cataracts, while in a unilateral cataract cases only 10 % are associated with heredity. 90 % of unilateral cataracts are considered sporadic, while only one third of bilateral cases are considered sporadic [40]. Understanding eye lens opacity mechanism, in the future could provide a key for etiology of idiopathic congenital and infantile congenital cataracts [27]. Diversity of inborn cataracts makes each IC case to be analysed as a unique system. In the current study, it is visibly seen by the comparison of different types of congenital cataract proportions, using Z test and by proving that in different cataract classification groups other classification type proportion ratios differ statistically significantly.

Studying pseudophakic eye postoperative complications in the selection – secondary glaucoma and secondary cataract, the obtained data, compared to the literature data, allows to argue on diagnostic possibilities, recognition of complications and possible errors. Secondary glaucoma after inborn cataract surgical correction, according to the literature data, is seen from 0 % to 32 % [6]. In the study, in the group of congenital cataracts 13.5 % cases at an early and/or late postoperation time developed secondary glaucoma in the pseudophakic eye. In the groups of infantile and juvenile congenital cataracts, secondary glaucoma was developed only in 2.04 % cases. In the randomised multicentre studies, as

mentioned in the literature 45ontro “Infantile Aphakia Treatment Study” (IATS) and “IoLunder2” study, secondary glaucoma was diagnosed more frequently. In the study “Infantile Aphakia Treatment Study”, “proved or suspected” glaucoma in IOL correction group developed in 28 % ($p = 0.55$) [23; 40]. The most common complication of paediatric cataract surgical correction by IOL implantation is lens reproliferation in the vision axis region [37]. In the study of 24 eyes of 57 (42 %) as described in “Infant Aphakia Treatment Study”, in which IOL was implanted, lens reproliferations developed [38; 39]. In the current study, very similar results were obtained: in 60 (42.65 %) of 138 eyes with pseudophakia secondary cataracts developed.

The objective of the current study was to investigate heterogenicity of congenital cataract and analyse how it influences eye refraction changes after congenital cataract surgical correction with IOL implantation.

The idea to correct aphakia by intraocular correction already at an early age had been thought of for long. Dr. Edward Epstein and Prof. D. Peter Choyce (UK) performed the first IOL implantation in children in the late 1950s [54]. Another literature source mentions that the first intraocular lens implantation in children was documented in 1951, the authors being Letocha and Pawlin [25]. At the beginning of the 21st century, IOL implantation was recognised to yield good results in children older than 2 years of age. In most countries around the world for any paediatric cataract surgeon this is a routine job [54]. Two comparatively recently published studies have introduced the evidence on 45ontrovers of IOL implantation and safety also in younger children [39; 40]. With the advance of IOL materials and design, advancement of technologies applied in cataract surgeries and surgical techniques, IOL implantation has become accepted and safe in many cases with much younger patients as it has been mentioned in one of the latest books on congenital cataract “Congenital Cataract. A Concise Guide to Diagnosis and Management” [27; 42]. Implanting an artificial intraocular lens into the eye with a certain refraction, there will form

initial pseudophakic eye refraction, which with the growth of a child and the eye is going to change. In Superstein et al. study published in 2002, pseudophakic eye myopic shift is 1.5 D in comparison to patients with aphakia whose myopic shift was 7.8 D. In the summary of the study the authors claim that a good strategy for intraocular lens calculations in pseudophakic patients would be initial postoperative emetropy [41].

Nevertheless, already initially based on observations of the eye growth and refraction changes in infancy and toddlers' age [10], as well as experience of congenital cataract treatment of aphakia [31], in pseudophakic cases hypermetropic IOL target refraction is grounded [53].

Greater changes in eye growth and myopisation occur in a child's first years of life and in the first months after birth. The wider and more different children's age during primary surgical correction time is included into the study group, the less precise and useless would the study results be. Therefore, in order to analyse the influential factors of eye refraction changes more correctly, in the current study just for the youngest child age – children up to 2 years –three separate groups of children ages were developed, when cataract extraction and IOL implantation has been performed surgically: from 1 to 6 months, from 7 to 12 months, and from 13 to 24 months (see Figure 2.8 a). Division into such small groups affects statistical analysis, decreasing the selection size and the study validity, yet it gives a chance to compare the eyes operated at similar ages, the size, growth abilities, refraction changes of which during the operation and after the operation will be similar.

The present study included 41 congenital cataract eyes operated at the age of 1 to 24 months. It was a part of the total selection of our study, which in total comprised 138 eyes of 85 patients, which were operated on from 1 months to 18 years of age. In the summarized VanderVeen table [47] (see Table 1.4) in the literature review of the thesis, there are encounted 11 studies in which myopic shift has been investigated in selections of congenital cataract patients operated

at an early age. When investigating the amplitude of selection and children's age in them, it can be traced that initially the authors had chosen to study all age children cataracts, while further on selections had been reduced, developing subgroups for patients up to 6 months, one or two years of age [47]. Concerning the size of myopic shift, the study results show similarity to the data of the current study, particularly if parameters of the 47ontrove groups were similar – the children's age during the operation and the observation time.

The results of all the studies prove that infants with congenital cataract after lensectomy and intraocular lens implantation during the surgery up to 2 years of age will develop myopic refraction changes at least from – 4 dioptries to – 10 dioptries. The present study, just in the same way as McClatchey [31], Lambert [20] and "Infant Aphakia Treatment Study" (IATS) [21], demonstrate that the earlier IOL implantation is done, the greater myopic shift develops. One should consider all benefits and shortcomings in pronounced myopic shift development cases [21; 26; 40].

The total selection was additionally divided in groups, which simultaneously was recording the time when the primary treatment was done and what the eye growth periods were (see Figure 2.8 a) and b). In the fast eye growth period (1–18 months) [10] the size of myopic shift median and dispersion were statistically significantly higher than in both slow eye growth periods and in the period when the eye stops growing any more (Leven test, $p < 0.05$). Statistically significant correlation was found in the current study between the eye axial length during primary surgical correction and pseudophakic eye refraction changes in myopic direction – myopic shift scope in the maximum observation period ($rs = 0.3$; $p = 0.01$, see Figure 2.10). Assessing standard deviations and dispersions of myopic refraction, congenital cataract eyes with different eye length during cataract extraction and intraocular lens implantation, a statistically grounded axial length threshold was acquired – 19 mm; to reach it in the operated congenital cataracts on the eyes during the growth of the child's eye, one could

observe big, unpredictable and dispersed eye refraction myopic shift. It can directly and precisely help clinicians who work with congenital cataract patients to decide which eyes to implant an intraocular lens in and which can be left aphakic, correcting the refraction error by contact correction method. In the eyes with AL < 19 mm and the eyes with AL ≥ 19mm, both MS median size and dispersion differed statistically significantly and markedly (see Figures 2.11 a and b and 2.12). In the current study the acquired data of eye length threshold are confirmed and grounded also in "Infant Aphakia Treatment Study", in which researchers mention eye axial length during the primary surgical correction time as a clinically significant expected error influential factor [48].

In relation to eye axial length during surgical correction, two groups were formed in the "Infant Aphakia Treatment Study"; in the first were the eyes < 18 mm, in the second > 18 mm. In the eyes, axial length of which during surgical correction was < 18 mm (27 eyes), the average expected error was 1.8 (2.0) D, while for the eyes > 18 mm (22 eyes), it was – 0.1 (1.6) D, p = 0.01 [48]. Comparable inaccuracy of IOL calculation formula create measurement difficulties of eye axial length at infancy and toddlers' age, as well as comparable inaccuracy of the contact A scan method and IOL calculation formula. Although several studies have been performed for the assessment of comparable inaccuracy of IOL calculation formula in children, the expected error for small eyes remains higher than in adults [2; 44]. If the congenital cataract eyes are studied, the length of which during the primary surgical correction is comparatively greater, the effect of eye axial length on the scope of myopic shift development and IOL target refraction expected error can also not to be found. For instance, in the article published in 2018 by group of Peru scientists, one cannot find any relationship between the initial eye axial length during the operation and myopic shift development three years after the operation [46]. In their study, congenital cataract eyes during the primary surgical correction were divided in two groups: with the eye axial length < 21.5 mm and the eye axial

length > 21.5 mm. Analysing the eyball length groups, it can be concluded that the first group (AG < 21.5 mm) includes all congenital cataracts operated on at the fast postnatal and slow infantile phase, and there are included children from 1 month of age to 5 years of age [10; 24]. Conclusions of the study authors can be opposed, mentioning that in the compared patient groups in the study congenital cataract eyes with very different characteristic values were included – different ages of children and eye axial 49ontro during cataract extraction time.

In the current study no comparison was performed; yet it could be interesting to compare the changes of eyeball lengths in different types of congenital cataract groups after 49ontrove extraction operation as the baby grows. Comparing the changes of eye axial lengths, Lambert et al. study "Infant Aphakia Treatment Study" mentions that the eye with a unilateral congenital cataract is shorter than a healthy eye. Axial length changes in the eye with contact correction were smaller than in eyes with intraocular correction [22]. Lorenz et al. in 1993 in their study "Ocular Growth in Infant Aphakia. Bilateral Versus Unilateral Congenital Cataracts" describe a bad correlation between eyeball length and eye refraction changes in bilateral congenital cataract cases. Thereby, mentioning the unpredictability as a drawback and not advising to correct congenital cataract eyes after cataract extraction surgical correction by intraocular correction [28]. Nowadays, 25 years later, other scientists also express more and more conclusions of similar type. In aphakia and contact correction cases there are observed at least two type reasonable shortcomings as well. If a contact lens gets lost, or caregivers stop using the contact correction, the infant aphakic eye refraction error can remain unchanged for a long time, which significantly increases the risk of amblyopia development. Contact lenses are expensive, and although they should be indicated only medically if the state or insurance do not reimburse them or the national health care system does not provide infants timely enough or lack constant follow-up in the postoperative period, refraction error correction cannot be performed. In aphakia shortcoming

there additionally should be included possible corneal inflammation, epithelial defects and ulcers which may develop in cases of longterm wearing of contact lenses [42].

Comparing myopic shift size of refraction changes in five chief congenital cataract morphological groups, a statistically significantly greater myopic shift was noticed in diffuse/total and nuclear cataract eye groups. To separate the influence of cataract onset time from the influence of morphological diversity, separate morphological analysis of different cataract groups at different cataract onset periods were done. As seen from the results, in Kruskall-Wollis statistical test analysis, in total/diffuse and nuclear IC morphology cases, myopic shift in different cataract onset time groups – congenital, infantile and juvenile – differ statistically significantly ($p = 0.01$), which proves the influence of cataract onset time. *McChatney et al.* in the early aphakic eye myopic shift studies mention, that inborn cataract morphological type and cataract onset time depend on each other and influence myopic shift size. He also reports that cataract morphology, secondary glaucoma, gender, laterality and best corrected vision acuity only slightly change myopic shift size, mentioning and proving that the early cataract surgery time [29] is the chief reason.

Thinking about laterality, the obtained data did not show any statistically significant myopic shift differences in the amplitude between the unilateral and bilateral cataract groups. In the literature myopic shift size in congenital unilateral and bilateral cataract operated on eyes has been studied repeteadly. Gouws mentions that spheric equivalent 36 months after cataract surgery was significantly more like myopic in unilateral cataract cases, in comparison to the cataract group [11]. McClatchey and Hoevenaar have come to similar conclusions [30; 13]. Lambert and colleagues report that the unilateral cataract surgery associates with a greater eye axial lengths extension rather than bilateral cataract surgery [22].

When investigating the influence of the treated congenital cataract complications on eye refraction change size, it was already in 1994 when the British congenital cataract group wrote that the secondary glaucoma increases eye refraction myopic shift size [1]. Comparing myopic shift size in patients with secondary glaucoma and without it in the current study, myopic shift median in patients whose primary cataract extractions and IOL implantation surgery was done at the age 1–6 months and who, after some time, developed secondary glaucoma, it was – 11.5 D, while median in the eyes, in which no secondary glaucoma was diagnosed in the same group was – 7.75 D. Unfortunately, the number of patients in the study group with secondary glaucoma was not sufficiently big to draw statistically significant conclusions.

Although secondary cataract also changes eye refraction error, in the studies on eye myopic shift the 51ontrover cataract was not mentioned as the fact affecting the myopic shift size. In the current study, neither in the first six months operated eyes, nor in the later period (7–216 months) operated eyes with secondary cataract, and without it, showed statistically significant myopic shift median changes (Mann-Witney test, $p = 0.70$), or any statistically significant dispersion (Leven test, $p = 0.45$).

Comparing myopic shift size of different treatment tactics groups – emmetropic and hypermetropic target refractions, dividing them more in detail according to the age in which cataract extraction and IOL implantation surgery were done, it was noticed that myopic shift size statistically significantly did not differ ($p > 0.05$) in different IOL target refraction groups < t different cataract extraction and IOL implantation ages. Although this conclusion was predictable, this part of the study is unique, since in any literature source the comparison of pseudophakic eye refraction changes in different IOL target refractions could be found. It shows that the target refraction does not affect myopic shift size and after IOL implantation the eye refraction will change from the initial refraction type and size. Different target refraction tactics can be partially equal to aphakia

correction with the contact correction or intraocular lens. In “Infant aphakia treatment study” it is described that in the contact lens group eye myopic shift was – 6.8 D, compared to – 9.66 D myopic shift in IOL group [21]. The greater myopic shift in pseudophakic eyes is associated with the higher optic power of intraocular lens. Lambert et al. in “Infant Aphakia Treatment Study” have drawn a conclusion that the chosen IOL power, together with the eye axial length increase and the correcting lens localisation (in a capsule bag, on retina or in the distance of glasses) affect myopic shift size. A greater IOL power will cause a greater myopic shift per one eye growth 52ontrovers [21]. In literature, however, any concrete correlation size difference in different infant age groups (2–6 months, 7–24 months) and the threshold could be found, when the correlation between myopic shift size and intraocular lens power would not be seen any more.

In the study, comparing myopic shift and implanted lens power in the eye groups, operated at different children’s ages, a negative correlation was observed between myopic shift and IOL power in the eyes, operated on till the child’s age of 2 years. After the operation at an early age from 1 to 6 months, IOL power increase by 1 D will cause a higher MS increase rather than if the operation is done from 7 till 24 months of age. The operated eyes at a later age were not seen to have an intraocular lens power and MS correlation.

To observe and understand refraction changes and a child’s vision development, a certain observation time is needed. The younger the patient at the time of IC surgical correction is, the more significant it will be. Different observation lengths can be explained by different IC patients’ ages during surgical correction, which calls for the possibilities and necessity of different observation lengths. The minimum observation/follow-up time in the current study was 6 months, the maximum – 120 months, the average follow-up time was 47.8 (SD = 37.21) months or 3.9 years. In the randomised multicentre study “Infant Aphakia Treatment Study” (IATS), the USA, the eye refraction changes,

complications, reoperations and vision development were compared 1 month after the operation and at the age of 5 years [21]. In "IoLunder 2" study, the association between IOL implantation and the vision acuity, secondary glaucoma like IC treatment complication was analysed 1 year after cataract surgical correction and IOL implantation [40]. VanderVeen paediatric cataract surgery experts Lloyed and Lambert published a book in 2017 "Congenital Cataract: A Concise Guide to Diagnosis and Management" giving a summarised table, which was adapted and published in the literature review of the Thesis (see Table 1.4), showing the observation periods of different authors. The minimum observation time in Lambert et al. published study in 1999 [20] was mentioned 1 year, the maximum observation time in McClatchey et al. published study in 2000 [31] was 3 years.

To overcome unequal observation time in the patients, the calculation was done of myopic shift per year in different IC surgical age groups. There is an average positive and statistically significant correlation between the children age groups during IC surgeries and the size of myopic shift per year ($rs = 0.062$; $p = 0.001$). The younger is the child during the operation, the higher will be the myopic shift per year. The older is the child during the operation, the more myopic shift is approaching 0. Myopic shift changes per year preserve the same tendency, shown by MS size changes in the selection during the maximum observation period.

It is worth to refer to two significant studies done lately, where congenital cataract aphakia correction is compared to contact correction or intraocular correction, the congenital cataract diagnosis, treatment, complications and vision prognoses are assessed. There are comparatively few studies on congenital cataracts; therefore, it is always a challange to study a rare disease at infant and children ages, in particular in such a small country as Latvia. In the randomised multicentre perspective study "Infant Aphakia Treatment Study" (IATS), the best refractive correction in children with congenital unilateral cataract was

assessed by drawing a conclusion that neither of these methods has any advantages [15]. “Infant Aphakia Treatment Study” and IOLu2 study highlighted a comparatively great number of perioperative and postoperative complications in infants in who IOL implantation had been done up to 6 months of age [38; 40]. Comparing the acquired vision acuity at 4.5 years of age in unilateral cataract patients, IATS did not point at any pronounced difference between the children whom aphakia was corrected by contact lenses, and the children in who intraocular lenses were implanted. IATS found that in the eyes with IOL implantation lens reproliferations occurred more frequently, causing vision axis opacity, and more commonly repeated surgeries were performed [15]. IOLu2 study investigated a big cohort of patients in the United Kingdom and Ireland with bilateral and unilateral congenital cataracts, in who cataract surgery had been done earlier than 2 years of age. Children with bilateral cataract operated on early, 1 year after the operation showed a tendency to have better vision results [40]. However, similarly to that of infant aphakia treatment (IATS) study, children with IOL implantations were seen to have a more frequent number of reoperations [38; 40].

If comparing the studies mentioned with the current study data on congenital cataract and pseudophakic eye refraction changes, initially several controversies can be found. The most common deals with intraocular lens implantation in children at an early age (1–6 months) which might be initially considered as improper and incorrect. And still, the selected congenital cataract method in Latvia and the study results should be defended, which are important both in the research of rare disease treatment and useful for clinicians, students and residents who are going to treat congenital cataracts or will learn and get to know this disease.

On the Paediatric Ophthalmology subspeciality day, September 21, 2018, organised by the World Society of Paediatric Ophthalmology and Strabismus, WSPOS president Prof. Ken K. Nischal admitted that “evidence-based studies

are not generally mandatory as guidelines in the whole world. Great importance here is each country's, region's, continent's social-economic state and possibilities of a particular health protection system. Each definite study indicates on the evidence-based results of a particular place and exact conditions" (Vienna, 21. 09. 2018, Paediatric Subspeciality Day organised by the World Society of Paediatric Opthalmology).

CONCLUSIONS

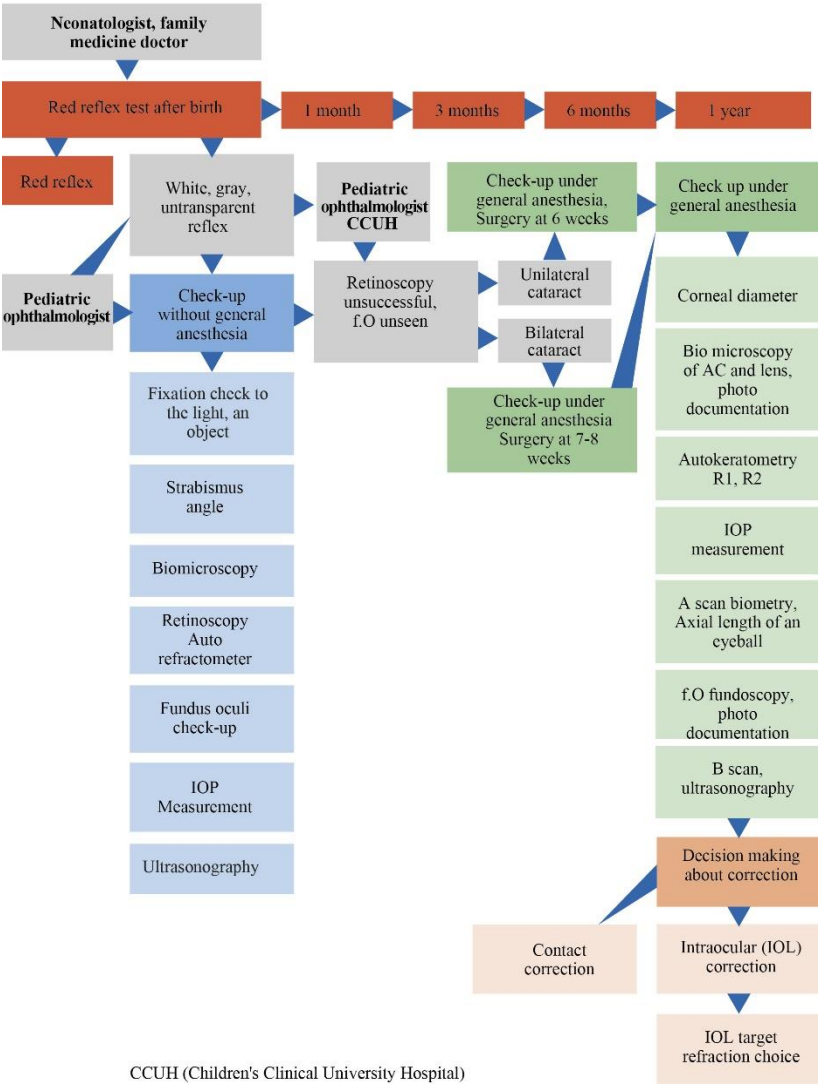
1. Inborn cataract is heterogenic and unique system, defined by different onset of cataract, morphology and laterality. These attributes affect the time of a surgery, type and refraction change – myopic shift.
2. Shorter axial length and earlier patient age at the time of a cataract surgery and intraocular lense implantation affects the change of an eye refraction – size and dispersion of myopic shift. If, at the time of a cataract surgery, a pseudophakic eyeball length is up to 19 mm, unpredictable dispersion of a refraction will appear, while the patient is growing. If pseudophakic eyeball length is 19 mm and more, refraction changes are more predictable and statistically less frequent.
3. Intraocular lense target different refraction tactics (emmetropy, hypemetrophy target IOL refraction) does not affect the size of myopic shift, although individual IOL refraction affects and correlates with myopic shift size.

PRACTICAL RECOMMENDATIONS

Recommendation No 1

Congenital cataract diagnosis and clinical eye investigation

For neonatologist, family physician, ophthalmologist,
paediatric ophthalmologist

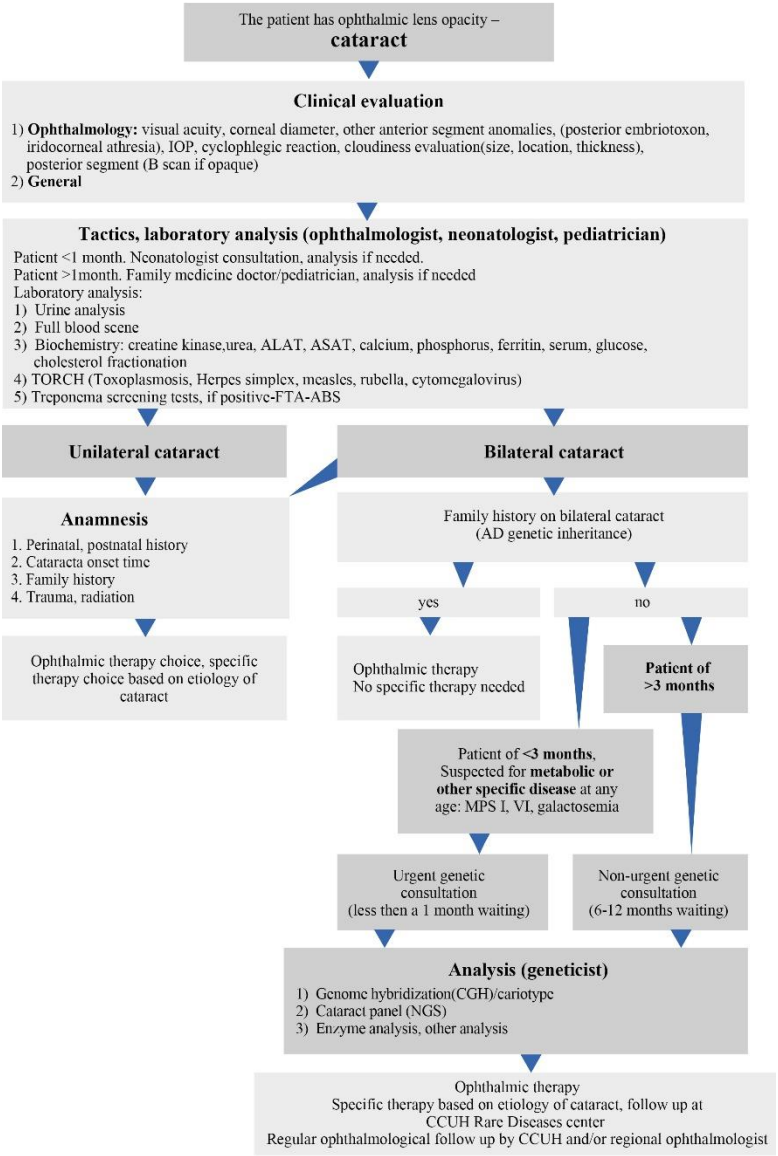


CCUH (Children's Clinical University Hospital)

Recommendation No 2

Clinical path in diagnosis of congenital cataract

For paediatric ophthalmologist, neonatologist, medical geneticist



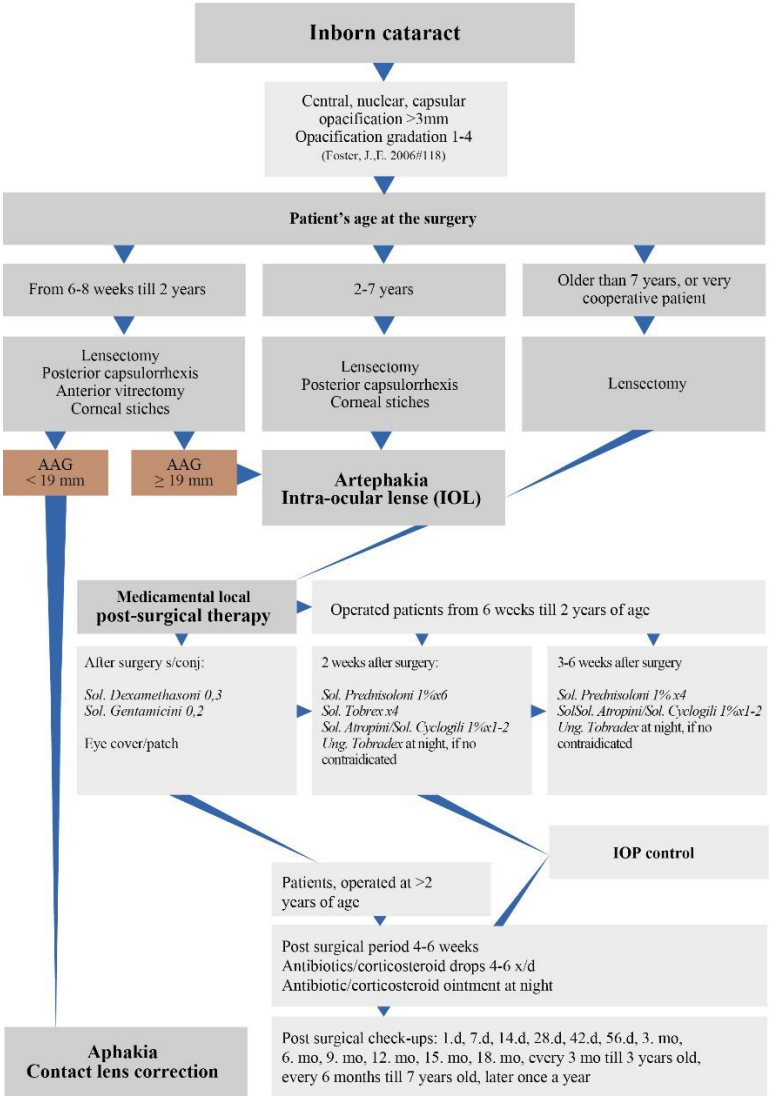
CCUH- Children's Clinical University Hospital

Recommendation No 3

Inborn cataract type of surgical correction in dependence of eyeball axial length during the cataract surgery

Postoperative medical treatment and follow up

For paediatric ophthalmologist and cataract microsurgeon



FURTHER PROSPECTIVE STUDY TRENDS

- The comparisson of the pseudophakic refraction changes for eyes with different axial lenghth during cataract extraction surgery in larger samples (multinational, multicentral reseach).
- Changes in eye axial length and corneal curvature in inborn cataract patients after cataract extraction surgery with and without IOL implantation, their correlation with eye refraction changes and myopic shift and its influencing factors.
- The influence of a child's age and type of operation on the development of secondary cataract.
- Development of vision, contrast vision and binocular vision in congenital cataract eyes after IK surgical correction, their influencing factors.
- Patching in bilateral and unilateral congenital and infantile cataract.
- Advantages and disadvantages of different vision correction types (monofocal, bifocal, progressive, contact correction) of a child's pseudophakic eye.
- Usefulness of classifications of ontology, HPO (Human Phenotype Ontology) and ORDO (Orphanet Rare Disease Ontology) for characteristics, examination and treatment of congenital cataract.
- Study of genetic causes of visually significant congenital cataract in Latvia.

APPROVAL OF THE DOCTORAL THESIS

Poster reports

1. Pētījums par iedzimtu kataraktu skrīninga metodi un iespējām (Eng. Study of the method and options for congenital cataract screening); *RSU Scientific Conference, 21.–22.03.2013., Riga.*
2. Prognosis for vision development in patients after childhood cataract surgery depending on cataract morphology, age of onset, IOL target power and post-operative complications. *40th EPOS Conference, 7–8.11.2014., Barcelona.*
3. Etiology of paediatric cataract in Children's University Hospital in Latvia. *40th EPOS Conference; 7–8.11.2014., Barcelona.*
4. Salīdzinošs redzes attīstības novērtējums pacientiem ar operētu iedzimto kataraktu atkarībā no kataraktas morfoloģiskā tipa, attīstības sākuma laika, implantētās IOL mērķa stipruma un pēcoperācijas komplikācijām. (Eng. Comparative assessment of visual development in patients with operated congenital cataract depending on cataract morphological type, starting time, implanted IOL target strength and postoperative complications) *RSU Scientific Conference, 26–27.03.2015., Riga.*
5. Myopic shift in children after intraocular lens implantation. *115th DOG Conference, 28.09.2017., Berlin*, DOG-2017 Travel Award.

Informative reports

1. Children lens abnormalities, reasons, diagnostic and treetment in Latvia. *107. DOG (Deutsche Ophthalmologische Gesellschaft) Conference;* 26.09.2009., Leipzig.
2. Iedzimtas kataraktas operāciju retrospektīva analīze. (Eng. Retrospective analysis of congenital cataract operations) *RSU Scientific Conference,* 19.03.2010., Riga.
3. Accuracy of intraocular lens power calculation in paediatric cataract surgery. *XIII Forum Ophthalmologicum Balticum, Vilnius, 21.08.2010.*
4. IOL aprēķini iedzimtu kataraktu ekstrakcijas ķirurģijā. (Eng. IOL calculations for congenital cataract extraction surgery) *RSU Scientific Conference*, 15.04.2011., Riga.
5. Postoperative refraction management in congenital cataract patients. *2nd Baltic Conference Paediatric Ophthalmology: the art and the science 2001. Lifelong benefits to child and family"*, 16.09.2011., Riga.
6. Strange cataracts, corneal and vitreoretinal lesions: suprising diagnosis. *XXXX Nordic Congress of Ophthalmology*, 26.08.2012., Helsinki, Finland.
7. Comparative analysis of vision development in patients with congenital cataract in relation to cataract surgery time and IOL target power. *XIV Forum Ophthalmologicum Balticum*, 24.08.2013., Tallinn.

8. Comparative assessment of vision development in patients with congenital cataracts depends on cataract morphology, cataract surgery time and IOL target power" *111th DOG Conference*, 20.09.2013., Berlin; DOG Travel Award.
9. Salīdzinošs redzes attīstības novērtējums pacientiem ar operētu iedzimto kataraktu atkarībā no kataraktas morfoloģiskā tipa, attīstības sākuma laika, implantētās IOL mērķa stipruma un pēcoperācijas komplikācijām. (Eng. Comparative assessment of visual development in patients with operated congenital cataract depending on cataract morphological type, starting time, implanted IOL target strength and postoperative complications) *RSU Scientific Conference*, 11.04.2015., Riga.
10. Treatment of childhood cataract within integral ethics. *41st EPOS Conference;* 26.06.2015., St. Petersburg.
11. Congenital cataract surgery and IOL implantation. Child's eye refraction changes. Baltic Eye Surgeons Talk Show. BEST VOL. 6., 25.08.2018., Jurmala.

Thesis

1. Valeiņa, S., Pastare, M., Klindžāne, M. Pētījums par iedzimtu kataraktu skrīninga metodi un iespējām (Eng. Study of the method and options for congenital cataract screening). *RSU Scientific Conference; 21–22.03.2013., 227 pp.*
2. Valeina, S., Sepetiene, S. Comparative analysis of vision development in patients with congenital cataract in relation to cataract surgery time and IOL target power. *XIV Forum Ophthalmologicum Balticum, Tallinn, 24.08.2013., 68 pp.*
3. Valeina, S., Sepetiene, S., Radecka, L., Vanags, J., Laganovska, G. Comparative assessment of vision development in patients with congenital cataracts depends on cataract morphology, cataract surgery time and IOL target power" *111th DOG Conference online thesis, Berlin, 19.–22.09.2013., 64 pp;* DOG Travel Award.
4. Valeina, S., Sepetiene, S., Laganovska, G., Vanags, J., Radecka, L., Erts, R. Prognosis for vision development in patients after childhood cataract surgery depending on cataract morphology, age of onset, IOL target power and post-operative complications. *40th EPOS Conference, Barcelona, 7–8.11.2014.; 101 pp.*
5. Valeina, S., Stūre, E. A. Etiology of paediatric cataract in Children's University Hospital in Latvia, *41st EPOS Conference, St. Petersburg, 26.06.2015.; 100 pp.*

6. Valeiņa, S., Laganovska, G., Radecka, L., Vanags, J., Erts, R. Salīdzinošs redzes attīstības novērtējums pacientiem ar operētu iedzimto kataraktu atkarībā no kataraktas morfoloģiskā tipa, attīstības sākuma laika, implantētās IOL mērķa stipruma un pēcoperācijas komplikācijām (Eng. Comparative assessment of visual development in patients with operated congenital cataract depending on cataract morphological type, starting time, implanted IOL target strength and postoperative complications). *RSU Scientific Conference, 11.04.2015., 227 pp.*
7. Valeina, S. Cure of childhood cataract within integral ethics. *41st EPOS Conference, St. Petersburg, 26.06.2015., 47 pp.*
8. Valeina S., Stūre E. A. Time of diagnosis, etiology and morphology of pediatric cataracts. *41st EPOS Conference, St. Petersburg, 26.06.2015, 67 pp.*
9. Valeina, S. Myopic shift in children after intraocular lens implantation. *DOG Conference, 28.09–1.10.2017., online thesis, 125 pp.*; DOG Trawel Award.

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1. Valeina, S., Sepetiene, S., Laganovska, G., Radecka, L., Vanags, J., Erts, R., Meskovska, Z., Sture, E. A. (2015). Analysis of Vision Development in Patients after Childhood Cataract Surgery, *Acta Chirurgica Latviensis, 15(1), 12–17.*
2. Valeina, S., Krumina, Z., Sepetiene, S., Andzane, G., Sture, E.A., Taylor, D. Fabricated or Induced Illness Presenting as Recurrent Corneal Lesions, Cataracts, and Uveitis; *J Pediatr Ophthalmol Strabismus [04 Feb 2016, 53 Online:e 6-e11](PMID:27007397).*
3. Valeina, S, Heede, S, Erts, R, Sepetiene, S, Skaistkalne, E, Radecka, L, Vanags, J, Laganovska, G. Factors influencing myopic shift in children after intraocular lens implantation. *European Journal of Ophthalmology, EJO-D-18-00722R1 |Accepted for publication on Dec 09, 2018 [EMID:21f8f03f75ef32d3].*

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