A Novel Congenital Cataract Category System Based on Lens Opacity Locations and Relevant Anterior Segment Characteristics

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PURPOSE. We compared the anterior segment characteristics of congenital cataract (CC) patients with lens opacities in different locations and proposed a modified, simple CC category system.

METHODS. Cataractous eyes of CC patients were classified into four groups based on the locations of lens opacities shown in slit-lamp examinations and by a 3-dimensional anterior segment imaging system as follows: total, anterior, interior, and posterior cataracts. The mean keratometry value, corneal astigmatism (CA), central corneal thickness (CCT), and anterior chamber depth (ACD) of eyes in different groups were compared.

RESULTS. We included a total of 428 CC patients. Half of the patients with an anterior cataract had the complication of a pupillary residual membrane. Among the patients with posterior lentiglobus cataracts, 90.38% had unilateral involvement. Patients with total, anterior, or interior cataracts had larger keratometry values than those with either posterior cataracts or clear lens. Congenital cataract patients had greater CA and CCT values than those with a clear lens. The largest CA was presented in patients with anterior cataracts, and the value decreased gradually with more posterior locations of lens opacities. Eyes with total and anterior cataracts had smaller ACDs, and eyes with interior and posterior cataracts had greater ACDs than eyes with a clear lens.

CONCLUSIONS. Cataractous eyes in CC patients with lens opacities in different locations presented distinct anterior segment characteristics. The modified CC category system, based on the relationships among the locations of lens opacities and anterior segment characteristics, may be beneficial for CC diagnosis and treatment.

Keywords: congenital cataract, category, locations of lens opacities, anterior segment characteristics
目的：比较具有不同晶状体混浊部位的先天性白内障患儿的眼前节参数，并根据比较结果提出一种更简便的改良版先天性白内障新分类系统。

方法：根据裂隙灯和三维眼前节成像分析系统的检查结果，将先天性白内障眼按照不同晶状体混浊部位分为以下四类：全白内障、前部白内障、中部白内障和后部白内障。分析比较各组具有不同晶状体混浊部位的白内障眼的角膜屈光度、角膜散光、角膜厚度和前房深度。

结果：本研究共纳入428名先天性白内障患儿，近一半前部白内障患儿合并瞳孔残膜，90.38%的后极圆锥白内障患者为单眼患者。全白内障、前部和中部白内障眼比后部白内障和透明晶状体眼具有更大的角膜屈光度。先天性白内障患儿的角膜散光和角膜厚度均大于正常透明晶状体眼。前部白内障眼的角膜散光最大，角膜散光随着晶状体混浊部位的后移而逐渐变小。相对于透明晶状体眼，全白内障和前部白内障眼具有更浅的前房深度，而中部和后部白内障眼则具有更深的前房深度。

结论：不同晶状体混浊部位的先天性白内障眼具有相异的眼前节参数。本研究根据晶状体混浊部位和眼前节参数关系提出的改良版先天性白内障新分类系统对先天性白内障的诊断和治疗具有重要的临床意义。

Congenital cataracts (CC) are the leading cause of childhood visual disabilities and treatable childhood blindness worldwide.¹ Congenital cataract patients have a wide range of presentations of lens opacities and generally are categorized into several groups based on the etiologies, anatomic locations, or shapes of lens opacities.²,³ Cataractous eyes of CC patients also frequently are complicated with other anterior segment abnormalities due to their close anatomic relationships and similar developmental origins. Lens opacities in different locations may be related to specific anterior segment abnormalities; for example, anterior polar cataracts are associated with greater corneal astigmatism (CA).⁴ However to our knowledge no studies have systematically related the locations of lens opacities to specific anterior segment abnormalities due to their close anatomic relationships and similar developmental origins. Lens opacities in different locations may help ophthalmologists predict the possible anterior segment abnormalities in CC patients. These abnormalities can be predicted simply based on the locations of lens opacities shown obtained through slit-lamp examinations without undergoing detailed biologic measurements, which is difficult for very young children due to a lack of cooperation. It is important for pediatric ophthalmologists to understand the relationship between the locations of lens opacities and specific anterior segment abnormalities in CC patients in general hospitals or temporary eye disease screening sites without biologic measurement equipment and safe sedation techniques.

Using the CC database in the Zhongshan Ophthalmic Center (ZOC),³ the current study compared the anterior segment characteristics of CC patients with lens opacities in different locations, and further proposed a modified CC category system based on the specific relationships between the locations of lens opacities and anterior segment character-
Statistics. Knowledge of these relationships is beneficial for further understanding of CC occurrence and development, and has clinical significance for CC diagnosis and treatment.

**PATIENTS AND METHODS**

**Subjects and Ethical Statements**

This prospective study was included in our series of ongoing studies at the Childhood Cataract Program of the Chinese Ministry of Health (CCPMOH), a national project for CC treatment and research. Congenital cataract patients less than 18 years of age and seeking treatment at the ZOC, a specialized eye hospital in South China, from February 2011 to December 2015 were candidates for this study. All included participants were diagnosed with CC before surgery and lacked other ocular abnormalities, such as severe corneal diseases, lens luxation, glaucoma, retinal diseases, nystagmus, nanophthalmos, and strabismus. All procedures adhered to the tenets of the Declaration of Helsinki and were approved by the Human Research Ethics Committee of the ZOC, Sun Yat-sen University. This study was performed after obtaining written informed consent from the legal guardian of each patient.

**Group Division and Anterior Segment Examination**

All subjects were examined thoroughly and diagnosed with CC independently by two experienced ophthalmologists (HTL and WRC). The analyzed eyes consisted of both eyes of unilateral cataract patients and a randomly selected eye of bilateral cataract patients. All selected eyes were categorized into five groups: total cataracts, anterior cataracts, interior cataracts, posterior cataracts, and clear lenses, based on the locations of lens opacities shown by a-slit lamp (BX900; HAAG-STREIT AG, Bern, Switzerland) examination and a 3-dimensional anterior segment imaging and analysis system (Pentacam HR; Oculus, Inc., Wetzlar, Germany) after mydriasis (Fig. 1; Table). For a more accurate categorization, the 3-dimensional images of each eye obtained by the Pentacam system were reviewed carefully (Fig. 2). The criteria for grouping were as follows: eyes with opacity of the entire lens were defined as having total cataracts; opacities limited to the interior of the lens without involving the anterior and posterior capsules were classified as having interior cataracts; lens opacities that involved the anterior or posterior capsules were classified as anterior or posterior cataracts; and the clear lens group consisted of healthy eyes of unilateral CC patients. Patients were excluded if the categorization of lens opacities was difficult or if bilateral cataract patients had asymmetric lens opacities in both eyes. The anterior segment parameters, including the mean keratometry value, CA, central corneal thickness (CCT), and anterior chamber depth (ACD), of CC patients were measured before surgery by the 3-dimensional anterior segment imaging analysis system described previously. Young patients who were unable to actively cooperate were examined after sedation with 10% chloral hydrate (0.8 ml/kg, oral or rectal administration).

**FIGURE 1.** Congenital cataract category based on the locations of lens opacities shown in slit-lamp and Pentacam examinations. Pentacam pictures are shown in the upper images, whereas the slit-lamp pictures are shown in the lower images.
Statistical Analysis

All measurements were analyzed using the Statistical Package for the Social Sciences (SPSS ver. 19.0; SPSS, Inc., Chicago, IL, USA). Absolute (n) and relative (%) frequencies were used to analyze qualitative variables, and means and standard deviations (mean ± SD) were used to analyze quantitative variables. The Kolmogorov-Smirnov test was used to evaluate the normality of the distribution of all variables. To control the effects of age on the CC categories comparisons, the differences between groups regarding the mean keratometry, CA, CCT, and ACD values were measured by covariance analysis. Analysis of Multiple Linear Regression (MLR) also was performed to further determine the degree of the correlation between position of lens opacities (the modified CC categories) and different anterior segment characteristics. A \( P \) value <0.05 was considered statistically significant.

RESULTS

We included a total of 428 CC patients. The mean age was 54.85 ± 42.28 months, and the ratio of males to females was 1.47:1 (255:173). Of these eligible patients, 34.81% (149/428) presented with a unilateral cataract, and the remaining 65.19% (279/428) had bilateral involvement.

To compare the anterior segment biometry characteristics of eyes with lens opacities in different locations, 598 eyes of 428 CC patients were classified into 5 groups as follows: total cataracts, anterior cataracts, interior cataracts, posterior cataracts, and clear lenses. The subgroups of interior and posterior cataracts are shown in Figure 3. Nearly half of the CC patients with anteriorly located cataracts (6/13, 45.15%) were complicated with pupillary residual membrane. Among patients with posterior lentiglobus cataracts, 90.38% (47/52) had unilateral involvement.

Comparisons of the specific parameters of the anterior segment of eyes with lens opacities in different locations are presented on average in Figure 4. Figure 4a shows that patients with total, anterior, or interior cataracts had larger keratometry values than those with either posterior cataracts or clear lenses. Furthermore, no differences in keratometry values between posterior cataracts and clear lenses were found. Congenital cataract patients had greater CA than those with clear lenses. Corneal astigmatism was significantly correlated with the locations of lens opacities; the greatest CA was present in patients with an anterior cataract, and the values decreased gradually as the lens opacities became more posterior (Fig. 4b). On average, a thicker cornea was found in eyes with any lens opacity (except for the anterior cataracts) than in eyes with a clear lens (Fig. 4c). Compared to the ACDs of eyes with a clear lens, eyes with total and anterior cataracts had smaller ACDs, while eyes with interior and posterior cataracts had larger ACDs (Fig. 4d).

To further determine the degree of the correlation between position of lens opacities and different anterior segment characteristics, analysis of MLR also was performed. The results of MLR are shown as follows:

![Figure 2. Typical 3-dimensional (3D) images of 4 types of cataracts with lens opacities in different locations. Sagittal views (in the first row), horizontal views (in the second row), and coronal views (in the third row) were included in each type of 3D image of cataracts. The red and green grids in every 3D image represent the front and back of the cornea, respectively. The upper and lower yellow grids under the green grids represent the front and back of the lens, respectively. The dark gray shape between the front and back of the lens indicates the lens opacity locations.](http://tvst.arvojournals.org/)

![Figure 3. Distribution of eyes with lens opacities in different locations. Eyes were categorized based on the locations of the lens opacities. Interior cataracts accounted for the largest proportion (39.13%, 234/598), whereas anterior cataracts accounted for the smallest proportion (2.17%, 13/598).](http://tvst.arvojournals.org/)
Congenital cataract is the leading cause of treatable childhood blindness and low vision worldwide.¹¹ Lens opacities in CC patients have a wide range of presentations and can be involved in each area of the lens due to their complex etiology. Cataractous eyes of CC patients also frequently are complicated with other anterior segment abnormalities due to their close anatomic relationships and similar developmental origins. However, no studies have reported the association of specific anterior segment abnormalities with the locations of lens opacities. In this prospective study with a relatively large sample size, we compared the anterior segment abnormalities of CC patients with lens opacities in different locations and proposed a modified CC categorization system. This study may be the first to compare the anterior segment parameters of eyes with CCs based on the locations of lens opacities. These important relationships are beneficial for further understanding of CC occurrence and development and are clinically significant for CC diagnosis and treatment.

Due to the close relationships in the anatomic position and embryonic development between the lens and other anterior segment structures, such as the cornea, we suspected that patients with lens opacities in different locations would have very distinct anterior segment parameters. However, few data have been published regarding these associations, mainly due to the small number of CC patients, the challenge of the

\[ Y = 2.66 - 0.35C_1 - 0.40C_2 + 0.13C_3 + 0.32C_4 + 0.004X \]

\[ P(C_1) \leq 0.001; P(C_2) = 0.004; P(C_3) = 0.009; P(C_4) \leq 0.001; P(X) \leq 0.001; \]

**FIGURE 4.** Comparisons of the anterior segment characteristics of CC patients with lens opacities in different locations. (a) Patients with total, anterior, or interior cataracts had larger keratometry values than those with either posterior cataracts or clear lenses. (b) Congenital cataract patients had a greater CA than those with a clear lens. (c) A thicker cornea was found in eyes with lens opacities compared to eyes with a clear lens. (d) Eyes with total and anterior cataracts had smaller ACDs, and eyes with interior and posterior cataracts had larger ACDs than eyes with a clear lens. Error bars: 95% confidence interval.

\[ \text{Km: } R = 0.144 \]

\[ Y = 42.67 + 0.72C_1 + 0.36C_2 + 0.60C_3 + 0.02C_4 + 0.003X \]

\[ P(C_1) = 0.013; P(C_2) = 0.561; P(C_3) = 0.946; P(C_4) = 0.008; P(X) = 0.122; \]

\[ \{C_1-C_4\} \text{[dummy variables of congenital cataract categories]: } C_1 \]

\[ = \text{Total cataracts, } C_2 = \text{Anterior cataracts, } C_3 = \text{Interior cataracts, } C_4 = \text{Posterior cataracts, Clear lens were set as a reference; } X = \text{age in months} \]

\[ \text{CA: } R = 0.342 \]

\[ Y = 1.25 + 1.30C_1 + 1.68C_2 + 0.74C_3 + 0.60C_4 - 0.002X \]

\[ P(C_1 - C_4) \leq 0.001; P(X) = 0.232; \]

\[ \text{CCT: } R = 0.173 \]

\[ Y = 541.05 + 35.92C_1 + 1.12C_2 + 16.20C_3 + 11.08C_4 + 0.002X \]

\[ P(C_1) \leq 0.001; P(C_2) = 0.955; P(C_3) = 0.018; P(C_4) = 0.18; P(X) = 0.98; \]

\[ \text{ACD: } R = 0.522 \]
necessary examination, and a lack of proper equipment. In the current study, which has a relatively large sample size (n = 428), we compared the anterior segment characteristics of eyes based on the different locations of lens opacities. The results show that cataractous eyes have different anterior segment parameters than eyes with a clear lens. Furthermore, the anterior segment abnormalities varied according to the specific locations of lens opacities. For example, cataractous eyes have larger CA and CCT values (on average) than eyes with a clear lens. The largest CA value was presented in patients with an anterior cataract, and this value gradually decreased as the location of the lens opacity became more posterior. Eyes with total and anterior cataracts also had a trend of smaller ACs, and eyes with interior and posterior cataracts had a trend of larger ACs than eyes with a clear lens. The results of MLR also showed the significant correlations between position of lens opacities and different anterior segment characteristics. The close anatomic relationships and the similar developmental origins between the lens and cornea may account for these associations. In humans, the lens placode is formed at a gestational age of 2 weeks and further invaginated to produce a lens pit after contact between the optic vesicle and the presumptive lens ectoderm. The lens pit then detaches from the surface ectoderm, which later develops into the cornea, and the lens vesicle is formed. More than 20 years ago, Bouzas found that six anterior polar congenital cataract patients presented with CA greater than 1.50 diopters. They inferred that the association of CA with this type of CC possibly was due to a delayed separation of the lens from the surface ectoderm during the early stage of fetal development. In addition to the greater CA and CCT values, we also found that nearly half of the CC patients with anterior lens opacity had the complication of a pupillary residual membrane. The stroma of the iris develops from the mesodermal tissues rich in blood vessels and is located between the surface ectoderm and lens. The thin tissue in the central stroma then regresses beginning at the sixth month of gestation and completely disappears by the eighth month. Any developmental abnormalities that occur during the regression process would contribute to pupillary residual membrane formation. Attachment between membranes and the front surface of the lens frequently occurs and may result in the co-occurrence of anterior cataract and pupillary residual membrane. Among patients with a posterior lentiglobus cataract, which is a special type of posterior cataract, more than 90% had unilateral involvement in this study. Mistr et al. reported similar findings, showing that all children with posterior lentiglobus cataracts had unilateral involvement and favorable outcomes. Knowledge of the relationship between the locations of lens opacities and specific anterior segment abnormalities in CC patients helps ophthalmologists predict possible anterior segment abnormalities and provides clinical significance for CC diagnosis and prognosis.

Based on the results of this study, we proposed a modified CC category system according to the locations of lens opacities, including total, anterior, interior, and posterior cataracts. The classification of a specific disease should aim to facilitate its diagnosis and treatment, and the newly proposed CC category system in the present study follows this principle. Congenital cataract patients previously have been categorized generally based on the etiologies, lenticular morphology, anatomic locations, and even the name of the investigating ophthalmologists or the family name of patients. Congenital cataracts were later classified into 11 types according to the genotype–phenotype correlation proposed by Reddy et al., including nuclear, lamellar, pulverulent, acceiform, cerulean, total, cortical, polymorphic, sutural, anterior polar, and posterior polar cataracts. However, these CC categories were complicated, aimed at academic research, and not effective for clinicians with a large workload. Furthermore, the traditional CC categories, such as the category system of Reddy et al., are lacking a detailed standard of classification, and mix up the position (such as nuclear cataracts and posterior polar cataracts) and the appearance (such as pulverulent cataracts and cerulean cataracts) of lens opacity. The newly proposed CC category system in the present study is concise and related to the characteristics of the anterior segment, which is more suitable and effective for clinical practitioners. The modified category system also would allow ophthalmologists to predict potential anterior segment abnormalities in CC patients with lens opacities in different locations and provide more directional advice with respect to the treatment and prognosis. In addition, traditional CC category systems usually classify cataractous eyes according to 2-dimensional examinations or images. For the purposes of accurate classification and analysis, the 3-dimensional images of all CC patients were considered for category assessment in the current study.

One limitation that should be noted is that because this was a preliminary study, some eyes with very complex morphologic characteristics that were difficult to classify were excluded. The anterior segment characteristics of these patients require further studies. Another limitation is that the application of the modified CC category system remains limited to one eye hospital in China; the clinical applicability of this modified CC category system requires further investigation by other eye care facilities located in different districts and with different medical levels. Another limitation should be concerned with the relatively large variations of results. However, the effects of variation could be minimized to some extent scientifically by the statistical method. Despite these limitations, this was the first study to our knowledge to compare the anterior segment characteristics of CC patients with lens opacities in different locations and to further propose a modified, simple CC category system accordingly. The

### Table: Detailed Anterior Segment Parameters of the Eight Representative Cases of Congenital Cataracts Shown in Figure 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Category</th>
<th>Locations of Lens Opacities</th>
<th>K Value, D</th>
<th>CA, D</th>
<th>CCT, μm</th>
<th>ACD, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Total</td>
<td>Whole lens</td>
<td>41.4</td>
<td>5.0</td>
<td>574</td>
<td>2.1</td>
</tr>
<tr>
<td>Case 2</td>
<td>Anterior</td>
<td>Anterior polar</td>
<td>42.7</td>
<td>2.5</td>
<td>623</td>
<td>2.8</td>
</tr>
<tr>
<td>Case 3</td>
<td>Interior</td>
<td>Nuclear</td>
<td>59.8</td>
<td>1.0</td>
<td>513</td>
<td>3.0</td>
</tr>
<tr>
<td>Case 4</td>
<td>Perinuclear</td>
<td></td>
<td>44.6</td>
<td>1.9</td>
<td>576</td>
<td>3.6</td>
</tr>
<tr>
<td>Case 5</td>
<td>Cortex</td>
<td></td>
<td>43.2</td>
<td>1.2</td>
<td>577</td>
<td>3.4</td>
</tr>
<tr>
<td>Case 6</td>
<td>Mixed opacities within the lens</td>
<td></td>
<td>41.6</td>
<td>0.8</td>
<td>590</td>
<td>3.8</td>
</tr>
<tr>
<td>Case 7</td>
<td>Posterior</td>
<td>Posterior subcapsular</td>
<td>42.9</td>
<td>0.6</td>
<td>555</td>
<td>4.1</td>
</tr>
<tr>
<td>Case 8</td>
<td>Posterior polar</td>
<td></td>
<td>44.3</td>
<td>0.3</td>
<td>561</td>
<td>5.1</td>
</tr>
</tbody>
</table>

K value, mean keratometry value; D, diopters.
distinctive 3-dimensional images of all cataractous eyes also were analyzed and considered for accurate categorization. Furthermore, the simplicity of the association between anterior segment characteristics and locations of lens opacities used in the modified CC category system may greatly facilitate and guide the clinical practice of CC diagnosis and treatment.

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References