Ocular Diseases on Naru Island, Japan: a Seven-year Survey

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Purpose: To examine the characteristics over seven years of ocular diseases in a closed society on Naru Island in Nagasaki Prefecture.

Subjects: Annual eye examinations were performed during routine physical examinations on Naru Island, Japan from 1995 to 2002. We examined 639 (213 males and 426 females) in 1995, 579 (196 males and 383 females) in 1998 and 421 (159 males and 262 females) in 2002.

Results and Discussion: Pterygium appeared to increase with age. The prevalence of cataract was higher in women than in men. Cataract was more prevalent in those with pterygium than in those without one. The prevalence of pseudoexfoliation increased with age, and it was greater in those with cataract than in those without one.

Conclusions: The incidence of degenerative and age-related diseases in this population followed for seven years showed a tendency to increase with age.

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Key Words: population-based study, Naru island, incidence of ocular diseases, prevalence of ocular diseases

Introduction

There are several eye studies of large populations: Framingham Eye Study, Massachusetts, US, Beaver Dam Eye Study, Wisconsin, US, Blue Mountains Eye Study, Australia, Barbados Eye Study, West Indies, National Health and Nutrition Examination Survey, US and Hisayama Eye Study, Japan. The diagnostic method, criteria and age range vary from study to study. These reports have greatly contributed to the analysis of factors related to prevalence, cause, progression, clinical features and relationship among diseases.

We examined the eyes of 10% - 14% residents of Naru Island annually from 1995 to 2002. Naru Island is an isolated off-shore island in Nagasaki Prefecture in western Kyushu, Japan. It is one of many isolated islands where the residents form a socially, historically, genetically and culturally specific society. Naru Island has a population of about 4,000 with no ophthalmologists.

The Naru Island Eye Study is a population-based study of ocular diseases, conducted by the Naru Town Office and supported by the Department of Ophthalmology of Nagasaki University Hospital. We examined for 7 years from 1995 to 2002 and recorded the prevalence, characteristics, and natural course of ocular diseases. We can study not only the prevalence but also the incidence of eye diseases. While association with risk factors can be estimated by cross-sectional data, incidence data are necessary to develop insights regarding potential causative factors. We studied the cumulative incidence of ocular diseases observed in the population from 1995 to 2002. Such a study is rare even in the above-mentioned population-based studies.

Subjects and Methods

Study population

In 1995, we examined 639 (213 males and 426 females) residents out of the total population of 4,674 (2,275 males and 2,399 females). In 1998, we examined 579 (196 males and 383 females) residents out of 4,396 (2,104 males and 2,292 females), and in 2002, we examined 421 (159 males and 262 females) residents out of 3,949 (1,895 males and 2,054 females).

In the analysis, we excluded those who were aged under 40 years or over 80 years at the time of examination. Thus, 612 (204 males and 408 females), 544 (182 males and 362 females) and 402 (147 males and 255 females) were remained for analysis among residents examined in 1995, 1998 and 2002, respectively.

Ethical approval for the study was obtained from the Naru Town Office and written informed consent was obtained from each resident we examined.
**Ophthalmic examination**

The examination included visual acuity, autorefractometry, applanation tonometry, slit lamp biomicroscopy, indirect ophthalmoscopy and non-mydriatic fundus photography, and was conducted by seven ophthalmologists. Applanation tonometry was performed on all individuals. A detailed high-magnification slit lamp biomicroscopy assessment of the anterior segment was performed. Pterygium was defined as the presence of a raised fleshy growth that crosses the limbus and encroaches onto the clear cornea. Individuals who had a history of pterygium surgery were included in the pterygium group. Slit lamp biomicroscopy was used to identify cataract. We estimated the angle width by van Herick’s method. Narrow angle was diagnosed when the ratio of anterior chamber to cornea was less than 1/3. Pseudoexfoliation was diagnosed by the presence of typical layered white deposits on the anterior lens surface. Increased cupping was diagnosed when the cup to disc ratio was larger than 0.5. Glaucoma was diagnosed by further examinations in the ophthalmology clinic. Ocular hypertension was diagnosed when tension exceeded 21 mmHg.

**Statistical analysis**

The prevalence and the cumulative incidence were analyzed for respective ocular diseases on the basis of logistic regression model with sex and age as covariates. Starting from the full model including interaction term of sex and age as well, we selected the most appropriate model by means of AIC. Once the most appropriate model was selected significance tests of parameters in the model were conducted using likelihood ratio statistics. Association between cataract and pterygium (or pseudoexfoliation) was analyzed in a similar way. FREQ, LOGISTIC and UNIVARIATE in the SAS- system were used for the calculations.

**Results**

The prevalence of ocular diseases by age is shown in Tables 1A, 1B and 1C, and the incidence of ocular diseases by age is shown in Table 2.

**Pterygium**

The prevalence of pterygium was 8.7%, 10.7% and 13.2% in 1995, 1998 and 2002, respectively (Tables 1A-1C), and showed a significant increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.03-fold (95% confidence interval, CI: 1.01-1.06) in 1995, 1.04-fold (95% CI: 1.01-1.08) in 1998 and 1.05-fold (95% CI: 1.02-1.09) in 2002, respectively.

The cumulative incidence of pterygium was 5.9% (Table 2). An increase in the odds of the cumulative

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**Table 1A. Prevalence of ocular diseases by age in residents of Naru Island, Nagasaki, Japan, examined in 1995**

<table>
<thead>
<tr>
<th>Ocular disease</th>
<th>Age at examination (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40-49</td>
<td>50-59</td>
</tr>
<tr>
<td>Pterygium</td>
<td>599 (13.7)</td>
<td>13560 (6.4)</td>
</tr>
<tr>
<td>Trichiasis</td>
<td>191 (2.8)</td>
<td>3140 (2.6)</td>
</tr>
<tr>
<td>Cataract</td>
<td>191 (2.8)</td>
<td>3140 (2.6)</td>
</tr>
<tr>
<td>Pseudoexfoliation</td>
<td>99 (1.3)</td>
<td>1570 (1.8)</td>
</tr>
<tr>
<td>Pseudophakia</td>
<td>99 (1.3)</td>
<td>1570 (1.8)</td>
</tr>
<tr>
<td>Enlargement of cupping of optic disc</td>
<td>139 (2.1)</td>
<td>2150 (1.9)</td>
</tr>
<tr>
<td>Glaucoma and ocular hypertension</td>
<td>139 (2.1)</td>
<td>2150 (1.9)</td>
</tr>
<tr>
<td>Narrow angle</td>
<td>99 (1.3)</td>
<td>1570 (1.8)</td>
</tr>
<tr>
<td>Angle-related macular degeneration</td>
<td>99 (1.3)</td>
<td>1570 (1.8)</td>
</tr>
</tbody>
</table>

**Table 1B. Prevalence of ocular diseases by age in residents of Naru Island, Nagasaki, Japan, examined in 1998**

<table>
<thead>
<tr>
<th>Ocular disease</th>
<th>Age at examination (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40-49</td>
<td>50-59</td>
</tr>
<tr>
<td>Pterygium</td>
<td>470 (4.7)</td>
<td>10368 (5.4)</td>
</tr>
<tr>
<td>Trichiasis</td>
<td>696 (1.1)</td>
<td>2160 (0.9)</td>
</tr>
<tr>
<td>Cataract</td>
<td>696 (1.1)</td>
<td>2160 (0.9)</td>
</tr>
<tr>
<td>Pseudoexfoliation</td>
<td>158 (2.6)</td>
<td>2550 (1.1)</td>
</tr>
<tr>
<td>Narrow angle</td>
<td>256 (4.3)</td>
<td>3850 (1.8)</td>
</tr>
<tr>
<td>Glaucoma and ocular hypertension</td>
<td>158 (2.6)</td>
<td>2550 (1.1)</td>
</tr>
<tr>
<td>Angle-related macular degeneration</td>
<td>158 (2.6)</td>
<td>2550 (1.1)</td>
</tr>
<tr>
<td>Angle-related macular degeneration</td>
<td>158 (2.6)</td>
<td>2550 (1.1)</td>
</tr>
</tbody>
</table>

**Table 1C. Prevalence of ocular diseases by age in residents of Naru Island, Nagasaki, Japan, examined in 2002**

<table>
<thead>
<tr>
<th>Ocular disease</th>
<th>Age at examination (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>40-49</td>
<td>50-59</td>
</tr>
<tr>
<td>Pterygium</td>
<td>245 (1.6)</td>
<td>1910 (1.0)</td>
</tr>
<tr>
<td>Trichiasis</td>
<td>645 (3.9)</td>
<td>2190 (2.2)</td>
</tr>
<tr>
<td>Cataract</td>
<td>645 (3.9)</td>
<td>2190 (2.2)</td>
</tr>
<tr>
<td>Pseudoexfoliation</td>
<td>135 (2.3)</td>
<td>2090 (2.3)</td>
</tr>
<tr>
<td>Narrow angle</td>
<td>645 (3.9)</td>
<td>2190 (2.2)</td>
</tr>
<tr>
<td>Glaucoma and ocular hypertension</td>
<td>645 (3.9)</td>
<td>2190 (2.2)</td>
</tr>
<tr>
<td>Angle-related macular degeneration</td>
<td>135 (2.3)</td>
<td>2090 (2.3)</td>
</tr>
</tbody>
</table>

- a) Number of examinee of residents examined (%).
- b) Number of cases/number of residents examined (%).

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incidence by 1 year increase in age was 1.03-fold (95% CI: 0.98-1.08) and was not statistically significant.

### Trichiasis

The prevalence of trichiasis was 1.8%, 1.7% and 2.5% in 1995, 1998 and 2002, respectively (Tables 1A-1C). A decrease in the cumulative incidence of trichiasis with age was observed (Table 2), but it was not statistically significant (odds ratio, OR=0.96, 95% CI: 0.89-1.03).

### Cataract

The prevalence of cataract was 30.6%, 43.0% and 37.8% in 1995, 1998 and 2002, respectively, and showed a significant increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.20-fold (95% CI: 1.16-1.25) in 1995, 1.20-fold (95% CI: 1.17-1.25) in 1998 and 1.23-fold (95% CI: 1.18-1.29) in 2002, respectively (Tables 1A-1C).

The cumulative incidence of cataract was 37.3% and a significant increase in the odds of the cumulative incidence by 1 year increase in age was demonstrated (OR=1.20, 95% CI: 1.15-1.26).

Table 3 presents the prevalence of cataract by sex and age in residents of Naru Island, Japan (1995-2002).

### Pseudoexfoliation (PE)

The prevalence of pseudoexfoliation was 3.3%, 4.8% and 3.7% in 1995, 1998 and 2002, respectively (Tables 1A-1C), and showed a significant increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.03-fold (95% CI: 0.98-1.08) and was not statistically significant.

### Pseudoexfoliation

The prevalence of pseudoexfoliation was 3.3%, 4.8% and 3.7% in 1995, 1998 and 2002, respectively (Tables 1A-1C), and showed a significant increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.03-fold (95% CI: 0.98-1.08) and was not statistically significant.

### Pseudoexfoliation

The prevalence of pseudoexfoliation was 3.3%, 4.8% and 3.7% in 1995, 1998 and 2002, respectively (Tables 1A-1C), and showed a significant increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.03-fold (95% CI: 0.98-1.08) and was not statistically significant.
increase in age was 1.09-fold (95% confidence interval, CI: 1.03-1.17) in 1995, 1.08-fold (95% CI: 1.03-1.14) in 1998 and 1.06-fold (95% CI: 1.0-1.13) in 2002, respectively.

The cumulative incidence of pseudoexfoliation was 3.5% and an increase with age was suggested (Table 2). However, the formal analysis indicated no significant increase with age (OR=1.03, 95% CI: 0.97-1.10).

Table 6 presents the prevalence of pseudoexfoliation by cataract. No significant difference was observed in the prevalence of pseudoexfoliation between residents with cataract and those without cataract in 1995 (p=0.66, chi-square test) and 1998 (p=0.12, chi-square test), while the prevalence of pseudoexfoliation was significantly higher in residents with cataract than in those without cataract in 2002 (p=0.001, chi-square test). The difference remained significant in 2002 after adjustment for sex and age (Table 6).

Table 6. Prevalence of pseudoexfoliation by cataract

<table>
<thead>
<tr>
<th>Year of examination</th>
<th>Cataract</th>
<th>Odds ratio* (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1995</td>
<td>7/187 (3.7)</td>
<td>13/425 (3.1)</td>
</tr>
<tr>
<td>1998</td>
<td>15/234 (6.4)</td>
<td>11/310 (3.6)</td>
</tr>
<tr>
<td>2002</td>
<td>12/152 (7.9)</td>
<td>3/250 (2.6)</td>
</tr>
</tbody>
</table>

* Odds ratio after adjustment for sex and age.

Narrow angle

The prevalence of narrow angle was 3.9%, 3.9% and 2.7%, in 1995, 1998 and 2002, respectively (Tables 1A-1C) and showed a trend to increase with age: an increase in the odds of the prevalence by 1 year increase in age was 1.07-fold (95% CI: 1.02-1.13) in 1995, 1.05-fold (95% CI: 1.00-1.11) in 1998 and 1.04-fold (95% CI: 0.98-1.12) in 2002, respectively.

The cumulative incidence of narrow angle was 4.69% (Table 2) and no significant correlation with age was observed (OR=1.01, 95% CI: 0.96-1.07).

Glaucoma and ocular hypertension

The prevalence of glaucoma and ocular hypertension was 1.5%, 2.4% and 3.5% in 1995, 1998 and 2002, respectively, and the cumulative incidence of glaucoma was 3.5%. Glaucoma with pseudoexfoliation was not found either in 1998 or 2002. However, one of the 612 residents (0.2%) examined in 1995 had the combined diagnosis.

Enlargement of optic disc cupping

The prevalence of enlargement of the optic disc cup was 6.4%, 6.4% and 5.7% in 1995, 1998 and 2002. The incidence of enlargement of the optic disc cup was 3.8%.

Chorioretinal atrophy

The prevalence of chorioretinal atrophy was 1.8%, 1.1% and 0.7% in 1995, 1998 and 2002, respectively, and the cumulative incidence of chorioretinal atrophy was 0.2%.

Age-related macular degeneration (AMD)

The prevalence of AMD was 0.3%, 1.1% and 1.0% in 1995, 1998 and 2002, respectively, and the cumulative incidence of AMD was 1.7%.

Diabetic retinopathy

Diabetic retinopathy was noted in 1 person (0.2%) of the 612 residents examined in 1995, in 2 (0.4%) of the 544 residents examined in 1998 and in 2 (0.5%) of the 402 residents examined in 2002.

Genetic diseases

Retinitis pigmentosa was found in 3 (0.5%) of the 544 residents examined in 1998 and in 1 (new patient, 0.2%) of the 402 residents examined in 2002.

Discussion

Many population-based eye studies have reported age differences in the prevalence of ocular diseases. However, we studied the prevalence and the incidence for 7 years on Naru Island. The characteristics of our examined population are unique. Naru Island is completely isolated and its population is decreasing, never increasing, and growing older year by year. The environment and occupations (fishing and farming) are unchanged. Thus this population is very suitable for a study of the natural course of certain age-related and degenerative diseases. Some diseases specific for the distinct are also discovered easily.

One of the prominent ocular diseases with a high prevalence on Naru Island was pterygium. Studies that included populations of all ages showed, the prevalence of pterygium to be 0.5% in South Africa,8)
The prevalence of pterygium on Naru Island increased apparently. The statistical significance was not shown in 1995 but was shown in 1998 and 2002. A similar tendency has been reported in several studies, although the prevalence of pterygium did not increase with age. An increase in the odds of the cumulative incidence by 1 year increase in age was 1.32-fold (95% CI: 0.86-2.12) and was not statistically significant. The age may not be a great risk factor for pterygium. Several studies reported an increased risk of pterygium with exposure to ultra-violet radiation. Such exposure has also been implicated as an increased risk of cataract. In our Naru Island Eye Study in 1998 and 2002, we found a statistically significant difference in the incidence of cataract in eyes with and without pterygium. In The Blue Mountains Eye Study, Australia, pterygium was associated with subcapsular cataract, but it was not associated with lens opacities in the Australian study by McCarty et al. in the Barbados Eye Study, West Indies or in the K Island Eye Study, Amami Islands, Japan.

The prevalence of cataract significantly increased with age in residents examined in 1995, 1998 and 2002, while a significant difference in the prevalence of cataract was not demonstrated between woman and man. A higher prevalence of age-related lens opacities in women than in men has been suggested in several studies. The Beaver Dam Eye Study reported that women were more severely affected with nuclear and cortical opacities than were men. The Barbados Eye Study reported that after adjusting for age, lens opacities were more frequent in women than in men. The possibility of hormonal effects on cataractogenesis needs further study.

The present study indicated a significant increase in the prevalence of pseudoexfoliation with age. Several population-based studies have reported that the prevalence of pseudoexfoliation increases with age. However, these reports are cross-sectional studies. An increase with age was suggested in the incidence of pseudoexfoliation (Table 2) though the increase was not statistically significant (OR=1.43, 95% CI: 0.78-2.78). The Framingham Eye Study, Massachusetts, US reported an association of pseudoexfoliation with senile lens changes but the association was not statistically significant. In the Naru Island Eye Study, a significant difference in the prevalence of pseudoexfoliation was shown between the residents with and without cataract who were examined in 2002. Taylor found a significant association between pseudoexfoliation and cataracts in Australian aborigines over 60 years of age. Since pseudoexfoliation and cataract are age-related, it would be probable that the observed association was due to aging.

Glaucoma with pseudoexfoliation was not found in the present study. It is very interesting that pseudoexfoliation was not associated with glaucoma on Naru. The same phenomenon has been noted by Toda in the Kamigoto Islands near Naru Island. The prevalence of pseudophakia increased in 7 years of the period of the present study (Tables 1A-1C). In 1995 when we started this examination, pseudophakia was 0.7%, but it was noted 3.2% in 2002. We recommended cataract surgery for those who had low visual acuity caused by cataracts. We are confident that the recommendation was valuable.

The prevalence of trichiasis showed no increase with age. A decrease in the cumulative incidence of trichiasis with age was observed but it was not the statistically significant. Trichiasis seems to have no association with age.

The prevalence of age-related macular degeneration (AMD) in white populations was 1.6% in the Beaver Dam Eye Study, Wisconsin, US 1.7% in the Rotterdam Eye Study, The Netherlands and 1.9% in the Blue Mountains Eye Study, Australia, while in black populations the prevalence of AMD was 0.6% in the

### Table 7. Comparison of prevalence of ocular diseases in main population-based studies

<table>
<thead>
<tr>
<th>Population-based study</th>
<th>cataract</th>
<th>diabetic retinopathy</th>
<th>AMD</th>
<th>glaucoma</th>
<th>PE</th>
<th>pterygium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Framingham</td>
<td>15.0%</td>
<td>2.1%</td>
<td>3.3%</td>
<td>1.5%</td>
<td>1.8</td>
<td>no data</td>
</tr>
<tr>
<td>Blue mountain</td>
<td>10.5%</td>
<td>6.5%</td>
<td>7.4%</td>
<td>10.3%</td>
<td>2.3</td>
<td>3.3%</td>
</tr>
<tr>
<td>Barbados</td>
<td>30.0%</td>
<td>5.0%</td>
<td>7.0%</td>
<td>10.3%</td>
<td>2.3</td>
<td>2.3%</td>
</tr>
<tr>
<td>Naru (1995)</td>
<td>20.0%</td>
<td>0.2%</td>
<td>1.0%</td>
<td>2.3%</td>
<td>1.5</td>
<td>3.7%</td>
</tr>
<tr>
<td>Naru (1998)</td>
<td>42.0%</td>
<td>4.0%</td>
<td>1.0%</td>
<td>2.3%</td>
<td>1.5</td>
<td>3.7%</td>
</tr>
<tr>
<td>Naru (2002)</td>
<td>35.0%</td>
<td>0.2%</td>
<td>1.0%</td>
<td>2.3%</td>
<td>1.5</td>
<td>3.7%</td>
</tr>
</tbody>
</table>

AMD: age-related macular degeneration. PE: pseudoexfoliation.
Barbados Eye Study, West Indies\textsuperscript{20} and 0.22\% in the Baltimore Eye Study, US.\textsuperscript{22} The prevalence of AMD in Hisayama, Japan\textsuperscript{17} was 0.87\%. The prevalence of AMD on Naru Island was 0.3\% in 1995, 1.1\% in 1998 and 1.0\% in 2002 and was similar to that of white populations.

The prevalence of diabetic retinopathy on Naru Island was 0.2-0.5\% over 7 years, which was much lower than that observed in several other studies (Table 7). The diet of Naru Islanders includes more fish and vegetables than meat.

Naru Island is completely isolated and the population is very stable. Thus genetic diseases may probably be present in some families. We found 4 patients with retinitis pigmentosa among those who received one examination during the 7 years, probably because of its long history and no possibility of treatment. In Japan the prevalence of retinitis pigmentosa is 1/4,000-1/6,000, so 4 patients in a population of about 4,000 population is very high, probably because of the geographically and historically closed society of Naru.

We examined the residents in Naru Island, Nagasaki Prefecture from 1995 to 2002 and found the changes in the prevalence of ocular diseases and recorded the natural course of several of them. We could obtain important information on the changes of ocular diseases with age, and we believe our Naru Island Eye Study contributes greatly to ophthalmological knowledge.

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References


