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THE PREVALENCE OF EYE DISEASES AMONG RESIDENTS IN AREAS IN NORTHEAST CHINA WITH HIGH AND ACCEPTABLE DRINKING-WATER FLUORIDE LEVELS

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ABSTRACT: *Purpose:* To investigate the difference in prevalence of seven common eye diseases in rural residents in Northeast China living in areas with high and acceptable levels of fluoride in the drinking water. *Methods:* All participants (rural residents aged ≥40 yr) underwent ocular examinations and tests related to the fluoride content of their drinking-water, including the fluoride levels in the blood, urine, and drinking-water, x-ray examination, and bone mineral density. The prevalence of seven common eye diseases were compared between subjects consuming drinking water with a high fluoride level, greater than the Chinese National Standard of 1.2 mg/L (exposed group), and those with an acceptable fluoride level of ≤1.2 mg/L (control group). *Results:* 1813 participants (766 in the exposed group and 1047 in the control group) were examined. The fluoride level in the drinking-water was closely associated with cataract (OR 0.543, 95% CI 0.310–0.845), pterygium (OR 1.991, 95% CI 1.931–3.622), and arteriosclerotic retinopathy (OR 2.011, 95% CI 1.121–3.637). Compared to the control group, there was a significant decrease in the exposed group of cataract (14.9% in exposed group, 24.7% in control group) and significant increases in the exposed group of pterygium (7.7% in exposed group, 3.2% in control group) and arteriosclerotic retinopathy (17.6% in exposed group, 6.4% in control group). *Conclusion:* This survey is the first study which has focused on the relationship between the fluoride level in the drinking-water and the prevalence of eye diseases. It provides epidemiological information that can be used in future in-depth studies.

Keywords: Age-related macular degeneration; Arteriosclerotic retinopathy; Cataract; China; Diabetic retinopathy; Drinking-water fluoride; Eye diseases; Fluoride; Northeast China; Prevalence; Primary angle closure glaucoma; Pterygium; Strabismus.

1 INTRODUCTION

Fluorine is one of the most common naturally occurring elements of the earth's crust and is present in the form of fluorspars which are usually composed of carbonates, calcium, fluoride, and sulfates.[1,2] It can be ingested by the human body from drinking-water, beverages, salt, and various kinds of food, etc. The fluoride concentration in water depends on manifold factors, including the minerals surrounding an aquifer, the pH, the reaction kinetics, and the time the groundwater has spent in the aquifer.[3-6]

Although the ingestion of low doses fluoride has been considered to be beneficial for preventing dental caries and strengthening bones,[7] fluoride is neither an essential trace element for human health nor necessary for the development of healthy teeth and bones.[8] Fluoride has many adverse effects on the human body when it is ingested chronically in a high dose, such as dental fluorosis, when it is ingested in childhood up to age 7 yr while the teeth are developing, skeletal fluorosis, and non-skeletal fluorosis.[9,10]

Fluorosis caused by exposure to a high fluoride level in drinking-water affects many countries of the world, especially the developing countries.[10] In the People's

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Republic of China, endemic fluorosis has been identified in 27 provinces located in areas of Northeast, Northwest, and Central China.[11]

In a survey of the literature, we did not find any study on whether or not a relationship existed between the intake of fluoride and the prevalence of eye diseases. Accordingly, this survey was designed to compare the prevalence of eye diseases in residents in areas with a high drinking-water fluoride level, greater than the Chinese National Standard of 1.2 mg/L, and in areas with an acceptable fluoride levels of ≤1.2mg/L).[12] The survey was carried out in February-July of 2014.

2 MATERIALS AND METHODS

2.1 Area selection and subject group selection: This study was approved by the Institutional Review Board of Harbin Medical University, Harbin, China. Eight villages of Daqing city and four villages of Tongyu city were selected as the exposed group, while four villages of Mudanjiang city were chosen as the control group.

The main reasons why these villages were chosen as study sites are as follows. Firstly, the villages of the two groups were similar in latitude, geography, and climatic conditions (Figure 1).

Figure 1. The locations of the study areas:
A: The four control group villages of Mudanjiang city (45°21'N, 130°17'E);
B: Four of the eight exposed group villages of Daqing city (44°87'N, 124°45'E);
C: The four exposed group villages of Tongyu city (44°70'N, 125°27'E);
D: The other four of the eight exposed group villages of Daqing city (44°46'N, 122°43'E).

They were remote, not close to major transport links, and situated at a similar distance to the nearest city, in which a good level of medical treatment was available. Secondly, the twelve villages of the exposed group were in the areas which were known to have a high level of fluoride in the groundwater. The household well water, without a defluoridation device, was the only drinking water source for the residents of these twelve villages. In contrast, the residents of the four control group villages were supplied by the same waterworks with drinking-water with ≤1.2 mg/L, in accordance with the National Chinese Standard of 1.2 mg/L.[12] Thirdly, most of residents in these villages of the two groups were engaged in farm production, so their labor strength, dietary habits, customs, and yearly incomes were similar. In addition, many villagers had a poor awareness of the treatment eye diseases and most of them had not undergone ophthalmologic examination.

Basic information (including sex, age, race, marital status, etc.) was obtained for all the residents of the two groups. The criteria used for selecting the subjects for the study from all residents were as follows: (i) were aged 40 years or older; (ii) were of Han nationality; (iii) had lived in the selected village for more than 10 years; and (iv) had an absence of congenital eye disease and ocular trauma.

2.2 Examination methods and the definition of eye diseases: All participants were underwent examinations associated with the fluoride content in the drinking-water including a blood sample test, a urine sample test, measurement of the fluoride content in the drinking-water, an x-ray examination, a bone mineral density assessment, etc., and ocular examinations, including near and distance visual activity test (2.5 meter standard logarithmic VA chart, Chinese GB 11533-2011), intraocular pressure (NIDEK Auto Noncontact Tonometer NT-2000), strabismus test (the cover-uncover test, prism and alternate cover test, and Krimsky test when necessary), slit lamp examination (YZ5J), dry eye-associated examinations (tear break-up time [tBUT], Schirmer I test [ST-I], and tear meniscus height [TMH]), fundus examination (Heine mini 2000), and noncycloplegic automated refraction examination (NIDEK AR-600A, NIDEK Corp, Japan). The presence of common eye diseases such as pterygium, cataract, primary angle closure glaucoma, arteriosclerotic retinopathy, diabetic retinopathy, age-related macular degeneration, and strabismus, were screened for by experienced eye doctors according to above ocular examinations.

2.3 Diagnostic criteria for the seven common eye diseases examined for in this survey: The following are the diagnostic criteria for the seven common eye diseases examined for in this survey. To clarify, as it was hard to carry weighty examination instruments to do a village to village survey, some ocular examinations, such as perimetry and fundus photography were not be done. We firstly had to screen out patients with suspected primary angle closure glaucoma, diabetic retinopathy, and age-related macular degeneration based on the available data. We then we took these patients who were suspected of having one of these diagnoses to our hospital to confirm the diagnosis through further examinations. This may have led to the prevalence we obtained for these three diseases being less than the true prevalence.

2.3.1 Pterygium: Pterygium was defined as the presence of a radially oriented fibrovascular encroachment which crossed over the nasal limbus (the border of the cornea and the sclera) and/or the temporal limbus.[13]

2.3.2 Cataract: Cataract was defined as any lens opacity in at least one eye. The total number of patients with cataract included the cases who had received cataract surgery and had pseudophakic eyes (eyes in which an artificial intraocular lens had been implanted) and aphakic eyes (eyes in which the lens is absent).

2.3.3 Arteriosclerotic retinopathy: Arteriosclerotic retinopathy was confirmed by direct ophthalmoscope examination and graded according to the Scheie classification for arteriosclerosis (Table 1).[14]

Table 1. The grade of arteriosclerotic retinopathy[a,14]

Stage	Observation
0	Normal
1	There is broadening of the light reflex from the arteriole, with minimal or no arteriolovenous compression.
2	Light reflex changes and crossing changes are more prominent.
3	The arterioles have a copper wire appearance, and there is more arteriolovenous compression.
4	The arterioles have a silver wire appearance, and the arteriolovenous crossing changes are most severe.

[a]Fundus examination was performed by an experienced ophthalmologist with a direct ophthalmoscope (Heine mini 2000).

2.3.4 Primary angle closure glaucoma (PACG): Primary angle closure glaucoma was identified on the available examination results in the survey (intraocular pressure, the limbal anterior chamber depth and cup:disc ratio) and the criteria of the ISGEO (International Society of Geographical and Epidemiological Ophthalmology).[15] The classification of PACG and the diagnostic criteria are summarized in Table 2.

Table 2. The classification of primary angle closure glaucoma (PACG) and the diagnostic criteria in this survey

Classification	IOP (mm Hg)	LACD/PCT	CDR
PACS	≤21	≤1/4	≤0.4
PAC	>21	≤1/4	≤0.4
PACG	>21	≤1/4	>0.4

Abbreviations: PACG: primary angle closure glaucoma; PACS: primary angle closure suspect; PAC: primary angle closure; IOP: intraocular pressure; LACD/PCT: limbal anterior chamber depth: peripheral corneal thickness ratio; CDR: cup:disc ratio.

2.3.5 Diabetic retinopathy (DR): Diabetic retinopathy was identified on the basis of a suspect having a history of diabetes and the presence of fundal changes due to diabetes. The fundal changes of DR included microaneurysms, intraretinal microvascular abnormalities, venous beading, retinal hemorrhages, soft or hard exudates, new vessels, fibrous proliferations, and macular edema.

2.3.6 Age-related macular degeneration (AMD): Age-related macular degeneration was identified as more than 2 drusen and/or obvious macular pigmentary changes within a radius of two discs diameter from the fovea.[16]

2.3.7 Strabismus: Strabismus was defined as constant or intermittent heterotropia at distance or near fixation. It was classified into esotropia (esodeviation=10prism diopters), exotropia (exodeviation=15 prism diopters) and vertical according to the primary direction. The cover-uncover test prism, the alternate cover test, and the prism test were used for identifying strabismus.[17]

2.4 Statistical analysis: All data were analyzed with SPSS 13.0 (SPSS Inc., Chicago, IL, USA). We analyzed the relation of fluoride exposure to seven eye diseases. We used a chi-square test to detect the difference between groups regarding the prevalence of eye diseases. Then, we used a multiple logistic regression model that assigned water fluoride concentration, sex, age, learning level, smoking status, alcohol consumption, blood glucose, and incomes as fixed factors, and eye diseases as the dependent variable, to explore the relationships between the fluoride exposure and the seven eye diseases. All the tests were two-tailed, and $P<0.05$ was considered to be statistically significant.

3 RESULTS

3.1 Characteristics of the study subjects: There were a total 766 subjects, aged 40 years or older, in the exposed group (including 286 male subjects and 480 female ones), and the mean age was 55.46±11.14 yr. There were total 1047 subjects, aged 40 years or older, in the control group (including 264 male subjects and 783 female ones), and the mean age was 58.42±9.20 years. The detailed socio-demographic characteristics of the study subjects are listed in Table 3. Except for gender composition ($P<0.001$), there was no significant difference between the two groups for the other the characteristics such as age, smoking and drinking habits, blood pressure, body mass index, education, and the annual income.

3.2 Associations between the fluoride level in drinking-water and prevalence of seven common eye diseases: The prevalence of seven common eye diseases according to sex are listed in Table 4 (the gender composition was a significant difference between two groups, so the prevalence was also calculated by gender). The prevalence (including total, male, and female prevalence) of pterygium and arteriosclerotic retinopathy in persons over the age of 40 years of age, in the high fluoride level drinking-water areas, was significantly higher than that in the control group, while the prevalence of cataract was lower in the subjects from the high fluoride level drinking-water areas than in the control group. The prevalence of the other four eye diseases (primary angle closure glaucoma, diabetic retinopathy, age-related macular degeneration, and strabismus) was not significantly different between the two groups.

Table 3. The socio-demographic characteristics of the study subjects

Characteristic	N (exposed group)	N (control group)	P value
N (subjects)	766	1047	
Sex			<0.001
Male	286	264	
Female	480	783	
Age (years, mean±SD)	55.46±11.14	58.42±9.20	0.367
Smoking			0.060
Yes	543	785	
No	222	262	
Drinking			0.272
Yes	482	685	
No	284	362	
Blood pressure (mean±SD)			
Systolic pressure	146.50±25.82	160.88±31.25	0.640
Diastolic pressure	84.78±13.36	78.08±8.42	0.080
Body mass index (mean±SD)	0.0030±0.0059	0.0026±0.0005	0.358
Education			0.917
Illiteracy	89	87	
Attended primary school	360	611	
Attended junior middle school	234	262	
Attended high middle school	57	87	
Attended college	26	0	
Annual income (yuan)			0.198
Less than 3,000	185	349	
3,000–5,000	47	0	
5,000–10,000	62	262	
10,000–30,000	192	262	
More than 30,000	280	174	

Table 4. Prevalence of seven common eye diseases in the exposed group and the control group

Disease	Group	Male[a] (%)	P[b]	Female[a] (%)	P[b]	Total[a] (%)	P[b]
Pterygium	Exposed group	10.5 (30/286)	<0.01	6.0 (29/480)	<0.01	7.7 (59/766)	<0.001
	Control group	4.2 (11/264)		2.9 (23/783)		3.2 (34/1047)	
Cataract	Exposed group	14.3 (41/286)	<0.01	15.2 (73/480)	<0.001	14.9 (114/766)	<0.001
	Control group	26.1 (69/264)		24.3 (190/783)		24.7 (259/1047)	
Primary angle closure glaucoma (PACG)	Exposed group	2.1 (6/286)	0.149	4.8 (23/480)	0.238	3.8 (29/766)	1.000
	Control group	4.5 (12/264)		3.4 (27/783)		3.7 (39/1047)	
Arteriosclerotic retinopathy	Exposed group	21.3 (61/286)	<0.001	15.4 (74/480)	<0.001	17.6 (135/766)	<0.001
	Control group	6.8 (18/264)		6.3 (49/783)		6.4 (67/1047)	
Diabetic retinopathy (DR)	Exposed group	2.1 (6/286)	1.000	2.1 (10/480)	1.000	2.1 (16/766)	1.000
	Control group	1.9 (5/264)		2.2 (17/783)		2.1 (22/1047)	
Age-related macular degeneration (AMD)	Exposed group	2.8 (8/286)	0.109	1.3 (6/480)	1.000	1.8 (14/766)	0.220
	Control group	0.8 (2/264)		1.1 (9/783)		1.1 (11/1047)	
Strabismus	Exposed group	0.7 (2/286)	1.000	0.2 (1/480)	0.263	0.4 (3/766)	0.374
	Control group	0.8 (2/264)		0.8 (6/783)		0.8 (8/1047)	

[a] Male = prevalence in males; Female = prevalence in females; Total = overall prevalence;
[b]P value and significance was associated at P<0.05.

3.3 Risk factors analysis of seven common eye diseases using multiple logistic regression model: The results of risk factor analysis are shown in Tables 5–8. The fluoride level in the drinking-water was closely associated with the prevalence of cataract, pterygium, and arteriosclerotic retinopathy (Tables 5 and 6). Fluoride exposure was a protective factor for cataract (OR 0.543, 95% CI 0.310–0.845), but was associated with an increased risk of pterygium (OR 1.991, 95% CI 1.931–3.622) and arteriosclerotic retinopathy (OR 2.011, 95% CI 1.121–3.637). The results of the risk factor analysis also showed that older subjects had a higher risk of suffering from these three diseases. Compared to those aged 40–49 yr, the residents aged 50–59 yr and over 60 yr had a higher OR for having cataract, pterygium, and arteriosclerotic retinopathy. In addition, subjects who had a smoking or drinking habit tended to have a higher pterygium prevalence; subjects with a higher annual income (more than 10,000 yuan) were more likely to have a lower pterygium prevalence; subjects with high blood glucose (≥6.39 mmol/L) had an increased the risk of suffering from arteriosclerotic retinopathy (OR: 1.711, 95% CI: 1.011–2.312).

Table 5. The associations between selected factors and cataracts, pterygium, and arteriosclerotic retinopathy

Fixed factors	Cataract		Pterygium		Arteriosclerotic retinopathy	
	OR	OR 95%CI	OR	OR 95%CI	OR	OR 95%CI
Sex						
Female	1.000		1.000		1.000	
Male	1.431	0.512–1.350	1.131	1.012–2.035	1.834	0.921–3.035
Age (years)						
40–49	1.000		1.000		1.000	
50–59	1.657	1.311–2.657	1.224	1.012–2.211	1.226	1.199–2.294
60–75	2.873	1.880–4.012	1.568	1.421–3.120	1.763	1.466–2.902
Drinking						
No	1.000		1.000		1.000	
Light	0.920	0.709–1.248	1.120	1.099–1.824	1.020	0.669–2.229
Heavy	1.280	0.932–1.691	1.216	1.142–1.919	1.166	0.643–2.901
Smoking (cigarettes per day)						
0	1.000		1.000		1.000	
1–9	0.743	0.612–2.334	1.023	1.015–4.123	1.320	0.465–4.224
≥10	1.174	0.758–3.231	1.974	1.654–4.876	1.466	0.546–4.944

Table 6. The associations between selected factors and cataracts, pterygium, and arteriosclerotic retinopathy

Fixed factors	Cataract		Pterygium		Arteriosclerotic retinopathy	
	OR	OR 95%CI	OR	OR 95%CI	OR	OR 95%CI
Education						
Illiteracy	1.000		1.000		1.000	
Attended primary school	1.342	0.891–2.205	0.943	0.982–1.205	1.094	0.982–1.205
Attended middle school	0.990	0.965–3.324	0.619	0.561–1.121	0.190	0.165–2.104
Attended college	1.321	0.802–4.453	0.434	0.302–0.931	1.134	0.102–1.231
Annual income (yuan)						
Less than 3,000	1.000		1.000		1.000	
3,000~5,000	0.947	0.818–3.432	0.754	0.718–1.654	0.147	0.118–1.123
5,000~10,000	1.713	0.819–3.465	0.834	0.819–2.324	0.134	0.119–1.124
10,000~30,000	2.132	0.523–4.261	0.638	0.502–0.896	0.138	0.102–1.162
More than 30,000	0.918	0.832–3.621	0.418	0.302–0.812	0.118	0.102–1.212
Blood glucose (mmol/L)						
3.84-6.38	1.000		1.000		1.000	
≥6.39	1.019	0.897–1.698	1.217	0.611–1.712	1.711	1.011–2.312
Water fluoride (mg/L)						
≤1.20	1.000		1.000		1.000	
≥1.20	0.543	0.310–0.845	1.991	1.931–3.622	2.011	1.121–3.637

Table 7. The associations between selected factors and primary angle closure glaucoma (PACG) and diabetic retinopathy (DR)

Fixed factors	PACG		DR	
	OR	OR 95%CI	OR	OR 95%CI
Sex				
Female	1.000		1.000	
Male	0.371	0.368–0.957	1.134	0.711–1.551
Age (years)				
40–49	1.000		1.000	
50–59	2.343	0.914–1.771	1.150	0.912–1.653
60–75	3.421	1.972–5.921	1.373	1.280–2.411
Drinking				
No	1.000		1.000	
Light	1.081	0.863–1.216	1.120	0.907–1.141
Heavy	0.611	0.327–0.641	1.382	0.991–1.196
Smoking (cigarettes per day)				
0	1.000		1.000	
1–9	1.059	0.907–2.993	1.142	0.812–1.153
≥10	0.824	0.399–2.069	1.271	0.858–2.139
Education				
Illiteracy	1.000		1.000	
Attended primary school	0.677	0.404–1.955	2.112	0.781–4.001
Attended middle school	0.736	0.209–1.999	1.980	0.661–2.451
Attended college	0.829	0.496–1.081	1.653	0.499–2.221
Annual income (yuan)				
Less than 3,000	1.000		1.000	
3,000~5,000	1.943	0.904–2.969	1.127	0.813–2.331
5,000~10,000	1.953	0.915–3.205	0.839	0.781–1.001
10,000~30,000	2.111	0.311–3.064	1.838	0.753–4.620
More than 30,000	1.447	0.931–1.246	0.881	0.732–2.112
Blood glucose (mmol/L)				
3.84-6.38	1.000		1.000	
≥6.39	1.491	0.933–1.694	1.231	1.092–1.987
Water fluoride (mg/L)				
≤1.20	1.000		1.000	
≥1.20	1.179	0.788–1.489	1.845	0.931–3.120

Table 8. The associations between selected factors and age-related macular degeneration (AMD) and strabismus

Fixed factors	AMD		Strabismus	
	OR	OR 95%CI	OR	OR 95%CI
Sex				
Female	1.000		1.000	
Male	1.424	1.111–2.589	1.073	0.668–1.657
Age (years)				
40–49	1.000		1.000	
50–59	0.850	0.711–1.958	1.343	0.869–2.076
60–75	2.321	1.821–4.541	1.301	0.772–2.192
Drinking				
No	1.000		1.000	
Light	0.920	0.877–1.843	1.592	0.973–2.846
Heavy	1.411	0.917–4.691	0.711	0.457–1.221
Smoking (cigarettes per day)				
0	1.000		1.000	
1–9	1.021	0.812–1.781	1.009	0.457–1.843
≥10	1.112	0.958–2.931	1.024	0.859–2.453
Education				
Illiteracy	1.000		1.000	
Attended primary school	1.085	0.681–1.715	1.485	0.897–2.455
Attended middle school	0.996	0.565–1.617	1.096	0.669–1.573
Attended college	1.118	0.662–1.893	0.778	0.498–1.200
Annual income (yuan)				
Less than 3,000	1.000		1.000	
3,000~5,000	1.246	0.802–1.994	0.746	0.446–1.254
5,000~10,000	1.534	0.939–2.559	0.953	0.620–1.665
10,000~30,000	1.202	0.760–1.982	0.985	0.587–1.464
More than 30,000	1.015	0.641–1.837	0.970	0.636–1.156
Blood glucose (mmol/L)				
3.84-6.38	1.000		1.000	
≥6.39	1.112	1.077–1.389	1.301	0.772–1.679
Water fluoride (mg/L)				
≤1.20	1.000		1.000	
≥1.20	1.048	0.735–2.221	1.598	0.936–2.689

The fluoride level in drinking-water was not a significant factor in the prevalence of the other four eye diseases (primary angle closure glaucoma, diabetic retinopathy, age-related macular degeneration, and strabismus) (Tables 7 and 8). However, age and blood glucose were associated with the prevalence of some of these four diseases: (i) the residents over 60 years of age had higher a OR of having primary angle closure glaucoma, diabetic retinopathy, and age-related macular degeneration, compared to residents aged 40–49 years; and (ii) the residents with a high blood glucose (≥6.39 mmol/L) tended to have a higher prevalence of diabetic retinopathy and age-related macular degeneration.

4 DISCUSSION

The results showed that the fluoride level in drinking-water was significantly related to the prevalence of cataract, pterygium, and arteriosclerotic retinopathy. We found the prevalence of these three diseases was significantly different in the subjects aged 40 or more years living in high drinking-water fluoride areas (>1.2 mg/L) compared to the subjects of the same age in the control group who lived in areas with an acceptable drinking water fluoride level (≤1.2 mg/L)

In the present study, one of the three diseases with a significant difference in prevalence in the two groups was cataract. Among the subjects over 40 years of age, the prevalence of cataract in the control group was higher than the prevalence in exposed group. The total cataract prevalence in the control group, aged over 40 years, (24.7%) was close to the prevalence reported in United States of 21.8%, but lower than that of 34.7% in Chinese residents, aged 40 years or more, in Singapore.[18,19]

It had been established that cataract prevalence is higher in lower latitude areas due to a higher UV index.[20] All the villages selected in this survey were located in higher latitudes with lower solar light intensities and the people in the northeast areas of China engage in fewer outdoor activities because of the cold climate in the winter. So the lower cataract prevalence found in this survey was probably because the UV index of these villages was lower than that in Singapore.

The cataract prevalence in the exposed group aged over 40 years was only 14.9% in total, 14.9% in males and 15.2% in females. This significantly lower value would be worth studying further to see whether a high fluoride level may play a role in the occurrence and development of cataract.

Another disease that was significantly different in prevalence was pterygium. The prevalence in the exposed group (7.7% in total, 10.5% in males and 6.0% in females) was higher than in the control group of subjects aged 40 or more years, and was similar to the 6.4% reported in a survey about pterygium in a Southern Harbin population.[21]

Various factors associated with pterygium have been reported such as genetic, infective, and immunological factors,[22] but there has not been any previous study about the relation between the pterygium and the fluoride level in drinking-water, Accordingly, further studies are also needed on this relationship.

We also found the prevalence of arteriosclerotic retinopathy was significantly different in the subjects aged 40 or more years in the two groups. In the high drinking-water fluoride areas, the prevalence of arteriosclerotic retinopathy was much higher, for the total, male and female groups, compared to the corresponding prevalences in the control group.

Arteriosclerotic retinopathy is considered to be the result of gradual calcification and a reduction of the elastic tissue of the blood vessels.[23] We noticed a study showing that an excessive intake of fluoride could lead to a change in the expression of type II collagen and its enhanced expression in rib cartilage tissues[24] and that this kind of collagen was absent at all levels of the retinal artery.[25] Based on these reports, we considered that the higher prevalence of arteriosclerotic retinopathy in the exposed group was related to the excessive intake of fluoride changing the expression of type II collagen in the retinal artery.

In addition, another related study revealed that fluoride toxicity could lead to hypocalcaemia which was inconsistent with the result of our survey where fluoride exposure was associated with increased arteriosclerotic retinopathy with increased calcification in the vessel walls.[26] So the occurrence of a higher prevalence of arteriosclerotic retinopathy in the high drinking-water fluoride areas may be calcium-independent.

Apart from the fluoride level in the drinking-water, the results of the risk factor analysis also showed that age was closely related to the prevalence of cataract, pterygium, and arteriosclerotic retinopathy. Older subjects tended to have a higher risk of suffering from these three diseases which is in accord with previous epidemiological reports.[27-29] Moreover, smoking, drinking, and annual income have been reported to be associated with pterygium,[30,31] and blood glucose has also been reported to be a risk factor for arteriosclerotic retinopathy.[32] The findings in our study supported these associations.

The prevalence of other four of the seven diseases (primary angle closure glaucoma, diabetic retinopathy, age-related macular degeneration, and strabismus) was not significantly different between the subjects, aged 40 or more years, in the two groups. However, the lack of an obvious difference does not mean that the fluoride level in drinking-water is unimportant in the prevalence of these four diseases. The study may have lacked sufficient power to detect a difference because the sample size may have been too small for conditions with a low prevalence such as age-related macular degeneration and strabismus.[33,34]

There were some limitations in our study. Firstly, the study had a cross-sectional design, and a long period of time is needed before the effects of high fluoride exposure on the human body become obvious. We therefore cannot conclude that any cross-sectional temporal association between fluoride exposure and the presence of eye diseases is causal. Secondly, the power of the study was limited with the sample size not being large enough for low prevalence diseases such as age-related macular degeneration and strabismus. Thus the levels of prevalence we found may possibly not be consistent with true prevalence of these diseases.

5 CONCLUSIONS

To the best of our knowledge, this survey is the first study which has focused on the relationship between the fluoride level in drinking-water and the prevalence of common eye diseases. The results of our work indicate that in addition to the known effects of excessive amounts of fluoride in drinking water of causing widespread pathological changes including dental fluorosis, skeletal fluorosis, and non-skeletal fluorosis, including increasing the risk of developing kidney diseases,[9,10] a high intake of fluoride may also act directly and/or indirectly on the eyeball and is significantly associated with some eye diseases. Our results provide epidemiological information that will be relevant for future in-depth studies on the relationship between fluoride and eye diseases.

6 CONFLICT OF INTEREST DECLARATION

No conflicting relationships existed for any of the authors.

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