The role of ethnicity in primary angle-closure glaucoma

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Primary angle-closure glaucoma is significantly more common than primary open-angle glaucoma in the East, whereas in Africa and Europe the reverse is true. In order to study the role of ethnic background in the frequency of primary angle-closure glaucoma in Cape Town and, in particular, in people of mixed ethnic background, the so-called 'coloureds', we retrospectively reviewed all patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital during a 30-month period. Primary angle-closure glaucoma was diagnosed in 11 of 63 (17%) whites, 11 of 85 (13%) blacks and 114 of 244 (46,7%) coloureds with primary glaucoma; the difference is statistically highly significant ($P < 0,001$). The human leucocyte antigen frequencies in 97 coloured patients with primary angle-closure glaucoma were similar to those found in a control group of individuals with a similar ethnic background. This study highlights the fact that coloureds are more predisposed to primary angle-closure glaucoma than whites or blacks. Because of their strong historical and genetic ties with south-east Asia, this greater prevalence of primary angle-closure glaucoma might be explained by an Eastern influence on the ocular structures of the eye, as opposed to an African or European influence.

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In western Europe and North America, primary angle-closure glaucoma is significantly less common than chronic open-angle glaucoma.[1-3] The situation is reversed in east and south-east Asia, however, where primary angle-closure glaucoma has been reported to be more common than primary open-angle glaucoma[3-10] (Fig. 1). It is interesting to note that the ethnic group with the highest prevalence of primary angle-closure glaucoma are the Eskimos, a Mongoloid people thought to be related to the people of east Asia.[3,11-13] The distinction between the two forms of glaucoma is important to the clinician, because the two conditions are treated differently.

In the western Cape the so-called 'coloured' people of mixed ancestry have strong genetic links with the East which can be traced back to the 17th century when the

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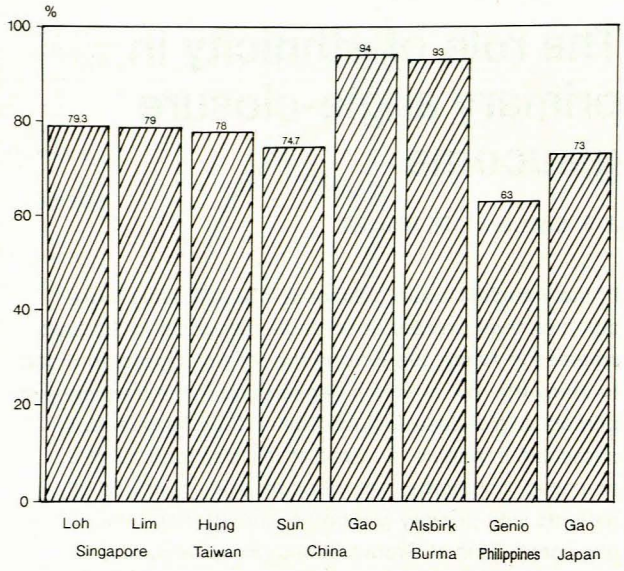

Fig. 1. Estimates of the relative frequency of primary angle-closure glaucoma among patients with primary glaucoma in Asia (hospital-based case series).

Cape was governed by the Dutch East India Company.[14] Their ancestors were mainly south-east Asians (from Indonesia and Malaysia) and indigenous Africans (Khoi-Khoi and San), and to a lesser extent east Africans (from Madagascar and Mozambique), west Africans and Europeans. They form an anthropologically distinct population, whose relatively recent origin is the result of early gene mixing at the Cape.[15]

We wondered whether because of their Eastern ancestry this group would show a greater predisposition to primary angle-closure glaucoma than whites or blacks in Cape Town. We therefore assessed all patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital during a 30-month period. The ratio of primary angle-closure glaucoma to primary open-angle glaucoma was determined in three distinct ethnic groups: whites, blacks and coloureds. In addition, the frequencies of the histocompatibility antigens were evaluated in 97 coloured patients with primary angle-closure glaucoma.

Patients and methods

All patients with primary glaucoma who attended the glaucoma clinic at Groote Schuur Hospital from July 1988 to December 1990 were retrospectively reviewed. Of the 392 patients, 244 (62%) were coloured, 85 (22%) were black and 63 (16%) were white.

Primary angle-closure glaucoma was diagnosed if the intra-ocular pressure was > 21 mmHg in the presence of a partially or totally occluded angle in at least one eye, and was made irrespective of the optic nerve appearance. Most patients had chronic angle-closure glaucoma.[16] Secondary causes of angle closure such as iris neovascularisation, lens intumescence and subluxation, trauma and uveitis were specifically excluded. Primary open-angle glaucoma was diagnosed if an open angle was found on gonioscopy in a patient with glaucomatous disc cupping and a corresponding visual field loss.

Human leucocyte antigens were determined in the 97 coloured patients with primary angle-closure glaucoma. HLA-A, -B and -C typing were performed by means of the NIH complement-dependent microdroplet lymphocyte toxicity technique.[17] B-cells, separated from peripheral blood by the nylon-wool method, were used for HLA-DR and -DQ typing performed by means of the technique agreed upon for the Seventh International Histocompatibility Workshop.[18,19] Local antisera as well as sera obtained by exchange with other laboratories were used. A control group was drawn from people with the same ethnic background and consisted of 3 716 individuals for the comparison of the HLA class I antigen frequencies and 549 individuals for the comparison of HLA class II antigen frequencies. Frequencies were compared between patients and controls at 16 A-locus, 29 B-locus, 8 C-locus, 10 DR-locus and 3 DQ-locus HLAs; the Chi-square test was used for proportions with Yates' correction. The *P*-values were multiplied by the number of comparisons made, as there was no prior reason to suspect that any significant differences would be found. A corrected *P*-value of <0,05 was considered statistically significant. The Chi-square test was used to compare the frequency of primary angle-closure glaucoma in the three ethnic groups.

Results

Primary open-angle glaucoma was almost twice as common as primary angle-closure glaucoma at this clinic. When the ethnic background of the patients was evaluated, it was found that 11 of 63 (17,5%) whites, 11 of 85 (12,9%) blacks and 114 of 244 (46,7%) coloureds had primary angle-closure glaucoma (Fig. 2). The prevalence of primary angle-closure glaucoma at this clinic was significantly greater in coloureds than in whites or blacks ($P < 0,001$).

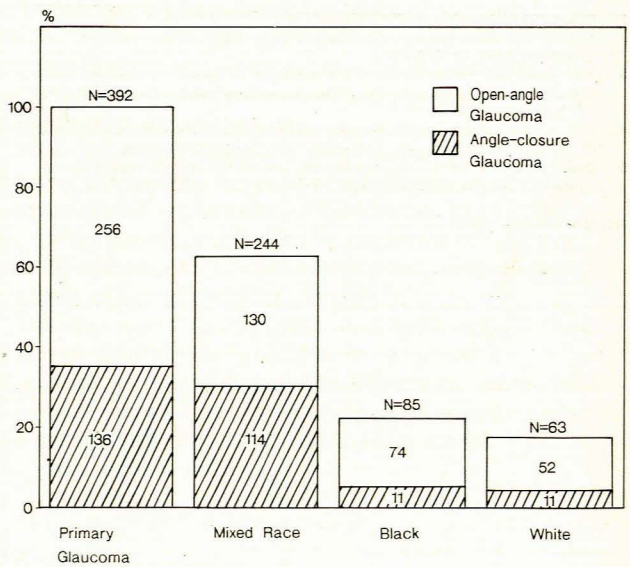

Fig. 2. Frequency of primary angle-closure glaucoma in three ethnic groups at the glaucoma clinic, Groote Schuur Hospital.

When HLA frequencies in patients and controls were compared, no statistically significant differences were noted between the groups (Table I).

Table I. HLA phenotype frequency in patients of mixed ancestry with primary angle-closure glaucoma, and controls

Antigen	PACG*		Controls		Yates	*P*-value
	Positive	Negative	Positive	Negative		
A1	21	76	610	3 106	1,5154	0,200 < *P* < 0,300
A2	24	73	1 160	2 556	1,5607	0,200 < *P* < 0,300
A3	14	83	552	3 164	0,0009	0,950 < *P* < 0,980
A10	20	77	559	3 157	1,8695	0,100 < *P* < 0,200
A11	17	80	469	3 247	1,6276	0,200 < *P* < 0,300
A23	4	93	427	3 289	4,4093	0,020 < *P* < 0,050
A24	23	74	701	3 015	1,1459	0,200 < *P* < 0,300
A28	16	81	586	3 130	0,0027	0,950 < *P* < 0,980
A29	5	92	326	3 390	1,1382	0,200 < *P* < 0,300
A30	16	81	679	3 037	0,0989	0,700 < *P* < 0,800
A31	2	95	84	3 632	0,0467	0,800 < *P* < 0,900
A32	1	96	220	3 496	3,2922	0,050 < *P* < 0,100
A33	7	90	242	3 474	0,0048	0,900 < *P* < 0,950
A36	2	95	32	3 684	0,4830	0,300 < *P* < 0,500
A43	7	90	207	3 509	0,2227	0,500 < *P* < 0,700
A74	1	96	140	3 576	1,2939	0,200 < *P* < 0,300
B7	14	83	756	2 960	1,6995	0,100 < *P* < 0,200
B8	8	89	350	3 366	0,0459	0,800 < *P* < 0,900
B13	3	94	147	3 569	0,0280	0,800 < *P* < 0,900
B14	10	87	255	3 461	1,2449	0,200 < *P* < 0,300
B15	16	81	440	3 276	1,5280	0,200 < *P* < 0,300
B18	12	85	367	3 349	0,4082	0,500 < *P* < 0,700
B22	2	95	42	2 456	0,0134	0,900 < *P* < 0,950
B27	6	91	172	3 544	0,2245	0,500 < *P* < 0,700
B35	16	81	425	3 291	1,8958	0,100 < *P* < 0,200
B37	2	95	64	3 652	0,0199	0,800 < *P* < 0,900
B38	2	95	91	3 625	0,0080	0,900 < *P* < 0,950
B39	3	94	143	3 573	0,0132	0,900 < *P* < 0,950
B41	3	94	161	3 555	0,1161	0,700 < *P* < 0,800
B42	3	94	231	3 485	1,1050	0,200 < *P* < 0,300
B44	14	83	627	3 089	0,2469	0,500 < *P* < 0,700
B45	4	93	198	3 518	0,0861	0,700 < *P* < 0,800
B46	0	97	4	2 494	0,8538	0,300 < *P* < 0,500
B47	4	93	79	3 637	0,9580	0,300 < *P* < 0,500
B48	0	97	3	2 495	1,3938	0,200 < *P* < 0,300
B49	0	97	70	3 646	0,9631	0,300 < *P* < 0,500
B50	3	94	22	3 694	5,6437	0,010 < *P* < 0,020
B51	7	90	182	3 534	0,6429	0,300 < *P* < 0,500
B52	10	87	148	3 568	7,9999	0,001 < *P* < 0,010
B53	3	94	96	3 620	0,0001	0,990 < *P* < 1,000
B57	12	85	313	3 403	1,4175	0,200 < *P* < 0,300
B58	6	91	614	3 102	6,6797	0,001 < *P* < 0,010
B60	3	94	166	3 550	0,1596	0,500 < *P* < 0,700
B61	7	90	178	3 538	0,7374	0,300 < *P* < 0,500
B70	8	89	580	3 136	3,3830	0,050 < *P* < 0,100
C1	3	94	125	3 591	0,0194	0,800 < *P* < 0,900
C2	8	89	609	3 107	4,0389	0,020 < *P* < 0,050
C3	11	86	586	3 130	1,0892	0,200 < *P* < 0,300
C4	33	64	866	2 850	5,4447	0,010 < *P* < 0,020
C5	2	95	141	3 575	0,3795	0,500 < *P* < 0,700
C6	33	64	1 162	2 554	0,2168	0,500 < *P* < 0,700
C7	40	57	1 536	2 180	0,0072	0,900 < *P* < 0,950
C8	10	87	259	3 457	1,1389	0,200 < *P* < 0,300
DR1	13	80	61	488	0,3908	0,500 < *P* < 0,700
DR2	39	54	189	360	1,6440	0,100 < *P* < 0,200
DR3	16	77	114	435	0,4234	0,500 < *P* < 0,700
DR4	21	72	117	432	0,0193	0,800 < *P* < 0,900
DR5	28	65	158	391	0,0189	0,800 < *P* < 0,900
DR6	22	71	113	436	0,2861	0,500 < *P* < 0,700
DR7	20	73	138	411	0,3864	0,500 < *P* < 0,700
DR8	6	87	29	520	0,0451	0,800 < *P* < 0,900
DR9	5	88	10	539	2,9842	0,050 < *P* < 0,100
DR10	3	90	9	540	0,3977	0,500 < *P* < 0,700
DQ1	71	22	363	186	3,3430	0,050 < *P* < 0,100
DQ2	28	65	149	400	0,2178	0,500 < *P* < 0,700
DQ3	50	43	240	309	2,8487	0,050 < *P* < 0,100

* PACG = primary angle-closure glaucoma.

Discussion

Previous studies have shown that the prevalence of primary angle-closure glaucoma is influenced by the ethnic background of the population studied[1,2,11-13,20-24] (Table II). In the East, primary angle-closure glaucoma is significantly more common than primary open-angle glaucoma.[3] In our glaucoma clinic, we had the opportunity to compare the relative frequency of this form of glaucoma in three distinct ethnic groups and, in particular, were able to determine the relationship between primary angle-closure glaucoma and primary open-angle glaucoma in people of mixed ancestry.

Table II. Prevalence (%) of primary angle-closure glaucoma in individuals over the age of 40 years in different ethnic groups (population-based studies)*

Country		Author	Prevalence
Wales		Hollows[1]	0,1
Sweden		Bengtsson[2]	0,1
Israel		Hyams[20]	0,5
Greenland	Eskimo	Clemmesen[11]	5,0
Canada	Eskimo	Drance[12]	2,9
Alaska	Eskimo	Arkell[13]	2,7
China		Hu[21]	1,3
Japan		Shiose[22]	0,3
South Africa			
Tswana		David[23]	1,0
Pondo		Bartholomew[24]	0,25
Coloureds		Salmon[30]	2,3

* Figures for America, continental Europe and south-east Asia are not available.

A diagnosis of primary angle-closure glaucoma was made in 17% of white and 13% of black patients with primary glaucoma. Although selection bias may play a role in our study, these figures correlate well with those from a 1973 Johannesburg study, when it was reported that 17% of blacks and 20% of whites with primary glaucoma attending the glaucoma clinic had primary angle-closure glaucoma.[25] These percentages are significantly lower than the 46,7% found in coloureds in this study.

The fact that coloured people are more likely to have primary angle-closure glaucoma than blacks and whites was noted in a 1964 study of the types of glaucoma treated at a Groote Schuur Hospital clinic.[26] Although the criteria for the diagnosis of primary angle-closure glaucoma are not recorded and no comment was made on ethnic differences in the frequency of primary angle-closure glaucoma in this early study, it can be calculated from the associated table that 68 of 112 (61%) coloureds, 23 of 98 (23,5%) whites and 8 of 41 (19,5%) blacks with primary glaucoma had primary angle-closure glaucoma.[26] This fact was not recognised by Mann[27] and was not included in a recent major review on the epidemiology of primary angle-closure glaucoma.[3]

Our study shows no differences in the histocompatibility antigen profile of patients with primary angle-closure glaucoma and controls. This indicates a lack of association between primary angle-closure glaucoma and histocompatibility antigens and supports the findings of Ritch[28] (20 patients) and Gieser[29] (35 patients) in the USA. It also confirms that the coloured patients in this study are significantly different genetically from white and black South Africans and that the sample of patients is representative of the ethnic background from which they were drawn.[15]

In conclusion, this study confirms that coloureds are significantly more predisposed to primary angle-closure glaucoma than whites and blacks. Because of their strong historical and genetic ties with south-east Asia, this predisposition might be explained by an Eastern influence on the ocular structure of these paients, as opposed to an African or European influence. The frequency of primary angle-closure glaucoma at a glaucoma clinic may not be the same as that in a population-based study.[3] For this reason, a prevalence study has been undertaken among the people of the village of Mamre, near Cape Town, and will be reported in detail in a separate study.[30]

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