Reappraisal of the ratio of disc to macula/disc diameter in optic nerve hypoplasia

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Abstract

The ratio of disc to macula/disc diameter is characteristically increased in eyes with optic nerve hypoplasia. We present the largest reported series of patients with a definitive diagnosis of optic nerve hypoplasia for whom this ratio has been determined. All measurements were made by an independent masked observer. Our results are in accordance with previous reports. A ratio of 2.94 provides a one-tailed upper population limit of 95%. An attempt has been made to correlate optic disc size and visual acuity. In 75% of bilateral cases the eye with the relatively smaller optic disc was found to have a better Snellen visual acuity than the fellow eye. This suggests that additional pathogenic mechanism(s) may have determined the eventual visual outcome in such eyes. Such mechanisms include macular hypoplasia, high refractive error, refractive amblyopia, central scotoma, and optic atrophy.

Underdevelopment of one or both optic nerves is a common anomaly.¹ The aetiology is unknown. Optic nerve hypoplasia (ONH) is a diagnosis which should be considered in any person with poor vision for which there is no immediately apparent explanation. Although the small optic disc of ONH is easily detected in severe cases, more subtle forms of the disorder may present more difficulty. The differential diagnosis includes the apparently small optic nerve head of hypermetropia. Subtle forms of the disorder may be difficult to distinguish from normal appearances. Red-free fundus photography can aid in this differentiation by detecting evidence of nerve fibre layer defects which correspond with that of the pattern of visual field loss.² However, many cases of ONH do not show such focal defects and are manifest solely as a uniformly thin nerve fibre layer within affected areas, which makes the condition more difficult to define than focal defects.³

Franceschetti and Bock⁴ measured the optic disc diameter by means of focal illumination of the fundus, using contact lens biomicroscopy and a micrometer scale. Estimation of the size of the optic disc by comparing the slit beam width on the Hagg-Streit 900 slit-lamp with the optic disc diameter on contact lens biomicroscopy has also been advocated.⁵ These relative measurements are useful in comparing the diameter of the optic disc relative to the slit-lamp beam or the scale, because their magnification when projected on the optic disc is assumed to be the same as the magnification of the optic disc, as the slit beam and microscope optics are parfocal and both pass through the optical system of the eye.

Other methods which have been described include comparison of the size of the optic disc with the size of the whole area of the fundus as seen in the standard fundus photograph,⁶ measurement with a scale over the frontal lens during indirect ophthalmoscopy,⁷ direct measurements of the orbital part of the optic nerve by CT scanning,⁸ A-scan ultrasonography,⁸ and B-scan ultrasonography.⁹

Variations in the size of the eye with concomitant differences in dioptric power even in emmetropic eyes render absolute measurement of intraocular structures difficult.^{10,11} Interference fringes provide a means of accurate measurement¹² but necessitate sophisticated equipment and a co-operative patient. The alternative is to make relative measurements from fundus photographs. The apparent size of the optic disc in fundus photographs is influenced by several factors, including the axial length, corneal curvature, and the shape of the fundus,¹³ and by refractive errors and optical aberrations, but because all photographed structures are equally influenced by anatomical and refractive variation such ratios are informative. Thus comparison of the optic disc diameter (DD) with the distance between the disc and macula (D-M) provides a useful index (D-M/DD ratio) of optic nerve head size. This assumes that the paired parameters normally bear a constant relation to each other. ONH has been said to be characterised by a ratio greater than 3:1.¹⁴⁻¹⁶

We have carried out a detailed study on patients with ONH^{17,18} and report our findings on the sensitivity of this technique employing the D-M/DD ratio on a cohort of patients with this condition.

Patients and methods

PATIENTS

The sources of patients were as follows: (1) The in-patient disease index of the Royal Hospital for Sick Children (RHSC), Glasgow; (2) the RHSC outpatient department diagnostic index maintained by the consultant staff; (3) Aberdeen Royal Infirmary, Scotland (with permission of the head of the department); (4) newly presenting cases (two patients with ONH and two with segmental ONH).

The patients thus identified were requested to attend for review. The unaided and corrected visual acuities were tested, and cycloplegic retinoscopy (half an hour after instilling 1% cyclopentolate eyedrops) was performed. The visual acuities were retested with correction whenever required. The D-M/DD ratio was identified according to the protocol outlined below. All eyes with non-segmental ONH had

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Figure 1 The appearance of the optic disc in ONH. The 'double ring' sign is demonstrated. An inner ring represents the borders of the optic disc (arrow), and an outer ring represents the outer border of the glial tissue.

subnormal uncorrected visual acuities. The 'double ring' sign, which is well described in the ophthalmic literature,^{8 19 20} was present in all eyes (Fig 1), except in the two eyes of patient 6. However, this patient had constriction of the visual fields to 5° from fixation, mental retardation, cerebral palsy, and hypothalamic dysfunction.

CONTROL SUBJECTS

Eighteen normal school children from a local school were tested after permission from the health authorities had been sought and consent of the parents had been obtained. All 18 children attended the clinic and together with three adult volunteers underwent visual acuity assessment, retinoscopy, and fundus photography according to the same protocol as the patients. The ages of the normal subjects ranged from 4 to 35 years (median 9, mean 10.47).

FUNDUS PHOTOGRAPHY

All patients and control subjects underwent bilateral fundus photography. One drop of 1% cyclopentolate eyedrops was used to dilate the pupils. Both colour and red-free photographs were taken in order to facilitate identification of the optic disc boundaries and foveal position in

difficult cases. Two colour (64 ASA Kodak Ektachrome) and two red-free colour fundus photographs (400 ASA Kodak Ektachrome) were taken with the same fundus camera (Canon CF-60 Z) at the 40° setting, and the clearest photographs were evaluated. In two cases (patients 6 and 20) 35° red-free fundus photography had been taken in Aberdeen Royal Infirmary (this does not, however, affect the determination of the D-M/DD ratio from these fundus photographs – see below).

IMAGE ANALYSIS

Fundus photographs were assessed by the VIDS V image analysis system (Analytic Measuring Systems Ltd). In every case the average disc diameter was calculated by adding the vertical and transverse disc diameters and then dividing by 2. The distance from the temporal margin of the optic disc to the fovea was measured from each photograph for both groups of subjects. Half the average diameter of the optic disc was added to this distance to obtain the 'disc-macula distance'. The disc-macula/disc diameter (D-M/DD) ratio was calculated for all patients and normal subjects. The same calibration technique was used for all the photographs studied. All the readings were taken and analysed separately by a masked independent observer (GND). The slides of the patients and of the normal control subjects had been mixed at random before they were analysed.

VISUAL ACUITY

The Snellen chart was used to test both the uncorrected and corrected visual acuities at a distance of 6 metres. The luminance of the Snellen test type was measured by a Solux SL 100 Lux meter; the mean screen luminance of six readings was 2900 asb. When young age or mental retardation resulted in inability to read the Snellen characters, the identity of the letters was sought by asking the subject to point to corresponding letters on a hand held Sheridan-Gardiner test form.

Table 1 Relationship of the visual acuity to the D-M/DD ratio in the patient group

Patient	Age	Sex	Unaided VA		Aided VA		D-M/DD ratio	
			OD	OS	OD	OS	OD	OS
1	4	M	0.5/60	3/60	0.5/60	3/60	3.23	4.00
2	4	F	6/18	6/12	6/18	6/12	3.04	?
3	8	M	1.5/60	6/36	1.5/60	6/36	6.08	4.60
4	17	M	6/60	6/60	6/60	6/24	3.26	3.61
5	21	F	*	*	*	*	3.44	3.85
6	19	F	6/60	5/60	6/24	6/18	4.08	4.24
7	11	M	3/60	6/60	6/60	6/36	?	3.67
8	3	M	*	*	*	*	3.45	3.53
9	2	M	1/60	6/9	1/60	6/9	3.87	?
10	15	F	6/36	6/18	6/18	6/12	?	4.40
11	16	M	6/9	6/24	6/7.5	6/12	2.80	?
12	6	M	3/60	6/60	3/60	6/60	3.32	3.67
13	14	M	6/60	6/36	6/60	6/36	2.91	3.58
14	7	M	6/36	6/60	6/36	6/60	?	3.48
15	7	M	3/60	1.5/60	3/60	1.5/60	?	3.26
16	26	F	6/7.5	6/7.5	6/6	6/6	2.68	3.14
17	4	M	6/60	6/36	6/60	6/36	3.44	3.28
18	19	M	6/12	6/7.5	6/7.5	6/6	3.22	3.32
19	4	M	6/12	6/18	6/12	6/12	3.47	3.10
20	43	F	†	6/18	†	6/12	?	3.06
21‡	9	F	6/6	6/6†	6/6	6/6†	3.33	2.72
22‡	22	F	6/7.5	6/6†	6/6	6/6†	3.27	2.71

*Blind eyes. †Eyes deemed to have no ONH. ‡Patients with unilateral right segmental ONH.
?=Not available. VA=visual acuity.

Results

Fundus photographs were taken for both eyes of 21 normal subjects by the same protocol. It was possible to determine the D-M/DD ratio for 40 eyes of 21 normal subjects. It was also possible to perform fundus photography in 41 eyes of 23 patients, including two patients with segmental ONH. However, in two eyes the quality of the photographs was poor, in two other eyes the fovea was not included in the fundus photographs, and in a further three eyes the fovea could not be located. Therefore measurements could be made to provide the D-M/DD ratio for 34 eyes of 22 patients (Table 1).

The mean D-M/DD ratio for the two eyes was taken as the datum value for a subject unless only one eye had been assessed, in which case the value for that eye was taken. The rationale for this type of analysis has been described previously.^{21 22}

The mean D-M/DD ratio for the normal

Table 2 Refractive errors of patients (reproduced with permission from the *British Journal of Ophthalmology* 1990; 74: 297-9)

Patients	TSP		Astigmatism*	
	OD	OS	OD	OS
1	1.62	1.12	0.25	0.75
2	3.12	3.12	0.25	0.25
3	2.00	2.12	0.5	1.75
4	-2.25	-0.87	6	3.25
5	0.12	0.00	1.75	1.5
6	1.37	2.62	0.75	2.75
7	1.25	1.12	4.00	4.25
8	1.62	0.5	1.25	1.5
9	2.25	2.12	0.5	0.25
10	-1.37	-1.37	4.25	4.25
11	1.25	0.75	0.5	0.5
12	1.12	2.37	2.75	2.25
13	0.5	0.37	2.5	2.25
14	1.5	2.5	1.5	2.5
15	0.25	-2.25	1.25	2.25
16	1.75	1.75	0.5	0.5
17	4.5	5.00	0.5	1.00
18	1.5	2.37	0.5	0.25
19	2.00	2.62	1.00	1.75
20	†	0.5	†	0.5
21*†	3.00	3.00†	0.00	0.00
22*†	1.75	1.75†	0.00	0.00

*In dioptres. †Eyes deemed to have no ONH.

‡Patients with segmental ONH. TSP=total spherical power.

group was 2.62. The mean ratio for the patient group was 3.57. As the data were found to be not normally distributed, an upper limit for the normal range was estimated by direct calculation of percentiles.²³ In view of the relatively small number of control subjects the most extreme limit which could be calculated was the 95% one-tailed upper population limit, which was 2.94. For only one patient (No. 11, who had bilateral ONH, but for whom only the right eye could be photographed) was the D-M/DD within this 95% limit for normal subjects; his D-M/DD ratio was 2.80. However, this patient showed the double ring sign in both eyes, and his corrected visual acuities were OD 6/7.5 and OS 6/12.

We looked at the visual acuity of the better eye in 12 patients with bilateral ONH for whom fundus photographs were available (blind eyes and eyes with segmental ONH were excluded) (Table 1). The visual acuities were compared with the D-M/DD ratios. No significant correlation was found (Pearson correlation coefficient, $p > 0.1$). Furthermore, in the eight patients with bilateral ONH for whom the D-M/DD ratio was calculated for both eyes, and for whom the visual acuities of the two eyes were different (patients 1, 3, 4, 6, 12, 13, 17, 18) six patients (75%) were identified in whom the eye with the better visual acuity had a relatively larger D-M/DD ratio than the worse eye (Table 1).

It is of interest that in 12 of 15 patients (80%) in this series, with bilateral ONH and asymmetrical corrected visual acuities, the left eye was the better eye. It is also noteworthy that for 10 out of 12 (83%) of the patients with bilateral ONH for whom the D-M/DD ratio could be determined for both eyes there was more astigmatism in the eye with the smaller D-M/DD ratio (the eye with the relatively larger optic disc) (Table 2). In only one patient was the degree of astigmatism less in the eye with the smaller ratio, and in one patient there was an equal degree of astigmatism of 0.5 dioptre in both eyes. This has been reported in detail elsewhere.¹⁷

Six patients (4, 6, 7, 10, 12, 13) had bilateral

asymmetrical ONH with a significant refractive error in the eye which had the smaller D-M/DD ratio. The visual acuities both with and without correction were the same in the eye with the better visual acuity for two of these patients (12 and 13). Visual acuities were improved with correction by more than one Snellen line in only two patients.

As for the two patients with segmental ONH, although the D-M/DD ratios for the affected eyes were significantly higher than for the normal fellow eyes, there was no impairment of visual acuity and no associated refractive error.

Discussion

The D-M/DD ratio is the ratio of the horizontal distance between the centre of the optic disc and the macula to the mean diameter of the optic disc, as evaluated from fundus photographs. This study presents the largest series of patients with ONH in whom this ratio has been measured. The second largest series comprised 19 eyes of 11 patients with ONH.¹⁵

The 95% one-tailed upper population limit of the D-M/DD ratio for the normal group in this study was 2.94. This indicates that in practice a ratio of 3 or more provides reliable supportive evidence for the diagnosis of ONH, and accords with previous reports.¹⁴⁻¹⁶ Awan¹⁴ selected the horizontal meridian only as an index for the disc diameter. Both Awan¹⁴ and Wakakura and Alvarez¹⁵ added half the transverse diameter of the optic disc to the distance between the fovea centralis and the temporal margin of the optic disc in order to calculate the disc-macula distance.

The pupils of only one patient (who was blind; no. 5) did not react to light. This absence of the pupillary light reaction indicates severe involvement of the light sensitive ganglion cells and the 'pupillary' fibres in the optic nerve as well as all the other ganglion cells, as this patient had no light perception in either eye.

The small size of the optic disc must be associated with the visual deficit in these patients. The following findings that indicate that additional factor(s) must contribute to the eventual visual outcome: (1) the visual acuities and the D-M/DD ratios were not significantly correlated in patients with bilateral ONH; (2) 75% of patients with asymmetrical bilateral ONH had a better visual acuity in the eye with the relatively larger D-M/DD ratio. Such factors may include the following.

Macular hypoplasia. In three eyes for which the photographs had been correctly exposed the position of the fovea could not be discerned in any of the fundus photographs, which therefore excluded them from further study. The visual acuities in these three eyes were hand movement in two and counting fingers in one. This suggests a degree of macular hypoplasia in these eyes, which may comprise features other than isolated absence of ganglion cells in the macula and their nerve fibres. Macular hypoplasia has not hitherto been described in association with ONH. However, histopathological study would be required to validate this hypothesis. In the two histopathological reports for patients blind with

ONH total absence of the ganglion cells and the nerve fibre layer has been documented in the affected retinae, but no comments were made on macular morphology.^{24 25}

Central scotoma. It was not possible to assess the visual fields in any of the patients who had poor corrected visual acuities. For one patient (no. 4) visuscopy indicated that an area temporal to the macula was employed for fixation by each eye. Both of these eyes had uncorrectable visual acuities despite high refractive errors. It is likely that in this patient eccentric fixation may have been caused by large central scotomata, perhaps due to underdevelopment of ganglion cells of the macula.

Refractive errors and refractive amblyopia. Refractive errors have recently been reported in association with ONH.¹⁷ In patients 7 and 10 there were high refractive errors in the better eyes, but the better eye of each of these patients improved by only one Snellen line by correction. An element of refractive amblyopia may therefore have contributed to impaired visual function in these two patients.

Optic atrophy. Optic atrophy and ONH are both manifestations of an 'insult' to the developing optic nerve. Therefore it is possible that the pale colour of the optic disc commonly seen in ONH is not due to a relative increase in the proportion of glial tissue (which is believed not to be affected in ONH), but is due to an absolute increase of the glial tissue and diminished vasculature in these optic nerves due to concomitant optic atrophy.

In conclusion, we recommend application of the D-M/DD ratio to assist in confirming the diagnosis of ONH. Simple measurements from fundus photographs are easy to carry out. In a child with bilateral ONH conclusions on the visual potential for an eye should not be drawn from the appearance of the optic disc alone. The diagnosis of ONH necessitates careful retinoscopy not only to exclude hypermetropia, but also to exclude associated astigmatic refractive errors in such patients, so that their visual development may be optimised.

Further research is required to explain the observation that several patients with ONH had no significant improvement in their visual acuities despite correction of high refractive errors. Further research is also required into concomitant mechanisms, other than the optic nerve size, which may impair the eventual visual outcome in some patients with bilateral ONH.

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