CORRELATION BETWEEN DISC DAMAGE LIKELIHOOD SCALE AND VERTICAL CUP DISC RATIO WITH AUTOMATED HUMPHREY PERIMETRY IN GLAUCOMA PATIENTS ATTENDING A TERTIARY CARE HOSPITAL, KATHMANDU, NEPAL

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ABSTRACT

Glaucoma is the second leading ocular disease of irreversible blindness. Glaucoma is a progressive disorder and requires serial evaluation in order to monitor disease progression and optimize therapy. The objective of this study was to determine the correlation between disc damage likelihood scale (DDLS) and vertical cup disc ratio (VCDR) with the results of Humphrey field analyzer (HFA) parameters. This study was a descriptive, cross-sectional and observational study. A total of 104 eyes of 52 patients diagnosed with primary open angle glaucoma or normal tension glaucoma were examined. DDLS staging, VCDR and HFA 24-2 visual fields were obtained from the patients. The correlation of DDLS and VCDR with Mean deviation (MD), Pattern standard deviation (PSD) and Glaucoma hemi field test (GHT) of HFA was calculated by Pearson correlation coefficient (r). DDLS showed a coefficient correlation value of r = -.628, r = .391 and r = .395 (p = <0.000) when correlated against HFA MD, PSD and GHT respectively. VCDR showed a coefficient correlation value of r = -.524, r = .317 and r = .221 when correlated against HFA MD, PSD and GHT respectively. DDLS has a better correlation compared to VCDR with all the parameters.

KEYWORDS

Glaucoma, disc damage likelihood scale, vertical cup disc ratio, visual field

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INTRODUCTION

Glaucoma is a progressive optic neuropathy characterized by loss of retinal ganglion cells and manifest clinically as loss of optic disc neuro-retinal rim tissue, localized or diffuse defects of retinal nerve fiber layer (RNFL) and deficits in functional visual field testing (VF). Optic disc (OD) evaluation is essential for the diagnosis as well as follow-up of glaucoma patients. The classification of the cup-to-disc ratio (CDR) was developed by Armaly for describing the optic nerve head (OND) in 1967.[1,2] The influence of the OD size or focal changes of the neuro retinal rim (NNR) were not taken into account by the CDR.[3] Large discs have larger CDRs (but may have normal neuro retinal rims) and therefore were more likely to be classified as glaucomatous.[3] Whereas smaller CDRs were more likely to be classified as normal, they also could already show glaucomatous damage to the ONH.[3] The NNR area reflect the number of ganglion cell axons passing through the optic disc and outperforms the CDR in its correlation with visual function. The disc damage likelihood scale (DDLS) was devised by Spaeth *et al*[4] to integrate the disc size and focal rim width into a clinical grading chart in 2002. DDLS showed a high inter observer reproducibility and correlates strongly with a degree of glaucomatous VF damage.[4] So, the objective of the study was to determine the correlation between each of DDLS and CDR with the results of HFA.

MATERIALS AND METHODS

The study was conducted in outpatient department (OPD) of Ophthalmology at Nepal Medical College Teaching Hospital (NMCTH) from January 2021 to December 2021. Sample size was taken using the formula finite size. One hundred and four eyes of 52 patients with enlarged vertical CDR ≥0.5 with focal thinning or notching of NNR with normal or raised intraocular pressure were included. This was a descriptive, cross sectional and observational hospital-based study. Patients with glaucomatous optic disc changes like vertically elongated optic cups, asymmetry of cup disc ratio (CDR) >0.2, thinning or notching of NNR, nerve fibre layer defect with normal or raised IOP were included in the study. Patients with secondary open angle glaucoma, who had undergone glaucoma surgery and patients with neurological diseases that could cause visual field defect were excluded from the study. Informed consent was taken from each patient.

Ethical clearance was taken from Nepal Medical College Institutional Review Committee (NMC-IRC). All patients received an ophthalmic examination including visual acuity, anterior segment by slit lamp examination, intraocular pressure measurement by applanation tonometry, central corneal thickness measurement by pachymetry, gonioscopy with single mirror goniolen and evaluation of the optic discs with +90 Diopter lens. All glaucoma patients were examined with Humphrey visual field using 24-2 Swedish Interactive Threshold Algorithm (SITA) threshold program of both eyes. Only the reliable (fixation losses <20%, false positives and false-negatives <33%) visual fields were included in the study. In case of unreliable fields, the test was repeated after few days. Then the more reliable field was selected for analytical purposes. Visual fields was considered to be abnormal according to Hodapp-Parrish-Anderson criteria.[5]

An abnormal visual field was defined as:

1. A glaucoma hemi field test (GHT) outside normal limits
2. Pattern standard deviation (PSD) p < 5% or
3. Three adjacent non-edge points p < 5% in the pattern deviation probability plot of which at least one point was p < 1 % and all points were on the same side of the horizontal meridian.

For this study, *mild glaucoma* was defined as a visual field defect corresponding to a mean deviation (MD) of −6 dB or better and vertical CDR ≤0.65, *moderate glaucoma* as an MD between −6 and −12 dB and vertical CDR 0.7 to 0.85, and *severe glaucoma* as an MD of −12 dB or worse and vertical CDR ≥0.9.[6]

The DDLS was determined by measuring the size of disc, drawing of the disc, the narrowest rim-to-disc ratio and the score. If the optic disc is smaller or larger than average size, then the DDLS score was adjusted appropriately. The disc was staged from stage 1 to 10 as from DDLS table. Disc size was measured using +90D lens at the slit-lamp. A slit beam was directed onto the disc and the graticule at the top was used to reduce the height of the beam until it corresponds to size of the disc. The figure in millimeter was multiplied by 1.33 as we used +90 D lens.

The DDLS staging and vertical CDR was recorded among the same glaucoma patients. Initially only recording of vertical CDR in glaucoma patients was done but now recording DDLS was also done as this is helpful in monitoring the progression of glaucoma.

THE DISC DAMAGE LIKELIHOOD SCALE

	Narrowest width of rim (rim/disc ratio)				Examples		
New DDLS Stage	For Small Disc <1.50 mm	For Average Size Disc 1.50-2.00 mm	For Large Disc >2.00 mm	Old DDLS Stage	1.25 mm optic nerve	1.75 mm optic nerve	2.25 mm optic nerve
1	.5 or more	.4 or more	.3 or more	0a			
2	.4 to .49	.3 to .39	.2 to .29	0b			
3	.3 to .39	.2 to .29	.1 to .19	1			
4	.2 to .29	.1 to .19	less than .1	2			
5	.1 to .19	less than .1	0 for less than 45°	3			
6	less than .1	0 for less than 45°	0 for 46° to 90°	4			
7	0 for less than 45°	0 for 46° to 90°	0 for 91° to 180°	5			
8	0 for 46° to 90°	0 for 91° to 180°	0 for 181° to 270°	6			
9	0 for 91° to 180°	0 for 181° to 270°	0 for more than 270°	7a			
10	0 for more than 180°	0 for more than 270°		7b			

Data was collected in research proforma. Data entry and statistical analysis were done using SPSS-20. The Chi-square test was used to find the association between categorical variables, whereas Pearson coefficient correlation (r) was done to find the correlation between DDLS and vertical CDR with the results of HFA parameters. P value <0.05 was considered significant.

RESULTS

Our study included 104 eyes of 52 patients with primary open angle glaucoma or normal tension glaucoma. The mean age was 54.23 ± 12.63 years ranging from 31 to 80 years with 32.7% of patients between ages 51-60 (Table 1). There was statistically significant association between age and DDLS stage (p = 0.044) but no significant association between age and vertical CDR (p = 0.97). Male patients were 28 (53.8%) and female were 24 (46.2%). There was no significant association between sex and DDLS and CDR (p = 0.558, p = 0.107). Regarding the ethnicity, Tibetomongolian were 33 (63.5%) and Indoaryan were 19 (36.5%). There was no significant association between ethnicity and DDLS and CDR (p = 0.184, p = 0.839).

In this study, 25 (48.1%) had no systemic illness,

Table 1: Demographic distribution and HFA parameters of glaucoma patients

Variables	Mean ± S.D
Age	54.23 ± 12.63
IOP	17.03 ± 3.51
CCT	532.47 ± 37.96
Disc size	1.85 ± 0.35
Vertical CDR	0.7:1 ± 0.12
Rim to disc ratio	<0.1:1
DDLS stage	5.2 ± 1.9
HFA MD	-8.80 ± 7.21
HFA PSD	4.87 ± 3.48

11 (21.2%) had hypertension, 10 (19.2%) had diabetes, 3 (5.8%) had both hypertension and diabetes, 2 (3.8%) had COPD and 1 (1.9%) had thyroid disease. There was no association between systemic diseases and DDLS and CDR (p = 0.33, p = 0.53).

The mean IOP was 17.03 ± 3.51 mm of Hg with range of 10 to 28 mm of Hg. The mean CCT was 532.47 ± 37.96 µm ranged from 420 µm to 614 µm

Table 2: Distribution of the DDLS in glaucoma patients	
DDLS Stage	**n (%)**
Stage 1-3	9 (8.7)
Stage 4-5	62 (59.6)
Stage 6-7	15 (14.4)
Stage 8-9	14 (13.5)
Stage 10	4 (3.8)

(Table 1). There was no significant association between IOP and CCT (p = 0.517). There was no significant association between IOP and DDLS (p = 0.134) but significant association between IOP and CDR (p = <0.000).

The mean vertical cup disc ratio was 0.7:1 ± 0.12, ranging from 0.5:1 to 0.95:1 (Table 1). According to cup disc ratio, mild glaucoma (CDR ≤0.65) was seen in 37 (35.6%) eyes, moderate glaucoma (CDR 0.7 to 0.85) was seen in 49 (47.1%) and severe glaucoma (CDR ≥ 0.9) was seen in 18 (17.3%) at the time of diagnosis. There was a statistically significant association between CDR and DDLS (p=<0.000) (Table 3).

Table 3: Association between vertical CDR and DDLS

	DDLS stage										
CDR	**1**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**	**p value**
≤ 0.65	1	6	18	8	4	0	0	0	0	37	
0.7-0.85	0	2	18	15	3	6	3	2	0	49	<0.000
≥ 0.9	0	0	3	0	1	1	5	4	4	18	
Total	1	8	39	23	8	7	8	6	4	104	

Table 4: Association between disc size and DDLS

	DDLS stage										
Disc size	**1**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Total**	**p value**
Small	0	0	0	4	4	1	0	1	1	11	
Average	1	4	22	19	4	6	6	4	3	69	<0.000
large	0	4	17	0	0	0	2	1	0	24	
Total	1	8	39	23	8	7	8	6	4	104	

Table 5: Pearson Coefficient Correlation between DDLS and CDR Vs HFA parameters

Comparative data	r value	P value	Type of relation
DDLS vs MD	-.628	<0.000	Moderate negative correlation
CDR vs MD	-.524	<0.000	Moderate negative correlation
DDLS vs PSD	.391	<0.000	Low positive correlation
CDR vs PSD	.317	0 .001	Low positive correlation
DDLS vs GHT	.395	<0.000	Low positive correlation
CDR vs GHT	.221	0.024	Very low positive correlation
DDLS vs VF defect	-.278	0 .004	Very low negative correlation
CDR vs VF defect	-.270	0.006	Very low negative correlation

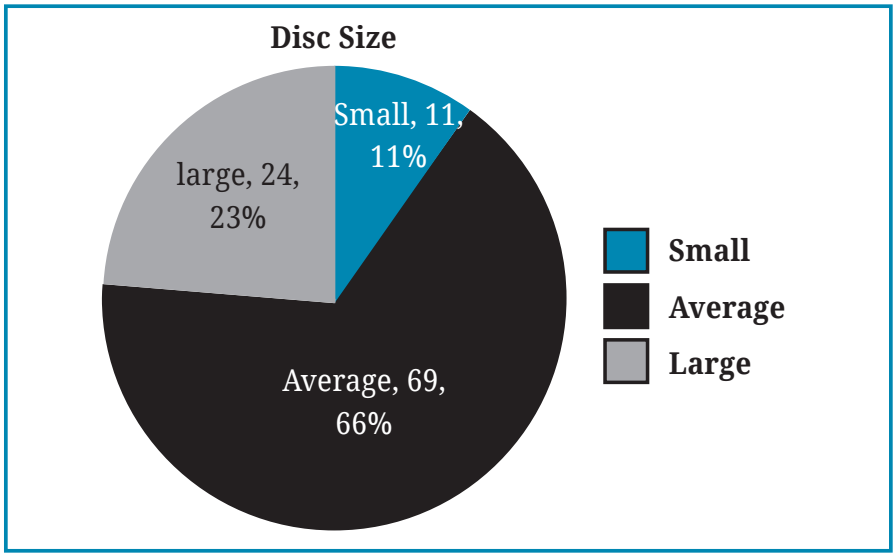

Fig. 1: Disc size variation among study patients.

Out of 104 eyes, 49 eyes had mild visual field defect, 34 eyes had moderate and 21 eyes had severe visual field defect which was statistically significant (p = <0.000).

Four (3.8%) eyes had sloping NNR, 71 (68.3%) had thinning and 29 (27.95) had notching NNR. There was statistically significant association between NNR and DDLS and CDR (p = <0.000, p = <0.000). Inferior NRR loss was seen in 35 (33.7%) eyes, temporal 19 (18.3%), superior 18 (17.3%), bipolar 15 (14.4%), inferotemporal 10 (9.6%), superotemporal 6 (5.8%) and nasal 1 (1%). There was significant association between NRR loss and DDLS and CDR (p = 0.007, p = 0.031).

The optic disc sizes were in ranges from 1.30 mm to 2.8 mm with average vertical disc size 1.85 mm ± 0.35. Out of 104 eyes, 11 (10.6%) had small disc size <1.5 mm, 69 (66.3%) had average disc size with 1.5 to 2.0 mm and 24 (23.1%) had > 2.0 mm disc size (Fig. 1). There was no statistically significant association between disc size and visual field defect (p = 0.966) but significant association between disc size and DDLS and CDR (p = <0.000 and p = <0.000) (Table 4). However, DDLS has low negative correlation with disc size (r = -.300, p = 0.002).

The mean rim to disc ratio was < .1:1. In this study, 42 (40.4%) eyes had <.1:1 rim to disc ratio followed by 28 (26.9%) who had .1:1 rim to disc ratio. There was a significant association between rim to disc ratio and DDLS and CDR (p = <0.000, p = <0.000). DDLS has very high positive correlation with rim to disc ratio which was statistically significant (r = .958, p = <0 .000).

The most common DDLS stage was stage 4 (37.5%) followed by stage 5 (22.1%) according to the new DDLS stage. The mean DDLS stage was 5.2 ± 1.9 in the present study. Nine (8.7%) eyes had DDLS stage 1-3, 62 (59.6%) eyes had DDLS stage 4-5, 15 (14.4%) eyes had stage 6-7, 14 (13.5%) had stage 8-9 and 4 (3.8%) had stage 10 (Table 2). The average mean deviation (MD) of HFA was - 8.80 dB ± 7.21, ranged from - 35.79 to - 0.58 dB. Out of 104 eyes 49 (47.1%) had MD < -6 dB, 34 (32.7%) had between -6 to -12 dB and 21 (20.2%) had > -12dB. When DDLS and vertical CDR was correlated with HFA MD, the result showed statistically significant, moderate negative correlation (r = - .628, p = <0.000 and r = -.524, p = <0.000) (Table 5).

In this study the mean pattern standard deviation (PSD) of HFA was 4.87 dB ± 3.48 ranged from 1.12 dB to 14.16dB. There was a low positive correlation between DDLS and PSD (r = .391, p = <0.000). Similarly CDR also had low positive correlation with PSD which was statistically significant (r = .317, p = 0.001) (Table 5).

Nineteen (18.3%) eyes had within normal limit, 21 (20.2%) had borderline and 64 (61.5%) had outside normal limit GHT in HFA. When DDLS was correlated with HFA GHT, it showed low positive correlation which was statistically significant (r = .395, p = < 0.000). Vertical CDR had very low positive correlation with HFA GHT which was statistically significant (r = .221, p = .024) (Table 5).

Visual field defect in HFA was present in 83 (79.8%) and absent in 21 (20.2%) eyes. There was a very low negative correlation between DDLS and CDR versus visual field defect (r = -.278, p = .004 and r = - .270, p = 0.006) which was statistically significant (Table 5).

DISCUSSION

Many patients show distinctive structural changes before detectable changes of the optic nerve head in the automated perimetry.[7] Furthermore, pathohistological findings have indicated that a large number of retinal ganglion cells need to be damaged before a noticeable abnormality is apparent on standard automated perimetry.[8-10] In the early stages of glaucoma the standard automated perimetry is likely to underestimate the impact that the damage will have on the ONH.[7,11] So the evaluation of CDR and DDLS are very important for diagnosis and monitoring the progression of glaucoma.

The two major advantages of DDLS are, firstly it considers the disc size and secondly it focuses attention on how much neuro retinal rim tissue is present. By categorizing discs as small, medium or large, the expectation of rim thickness is adjusted. This reduces the misclassification bias based on the disc size. It also takes into consideration the focal loss of rim tissue. Hence two eyes with same rim areas may have different DDLS stage if one has a focal rim tissue loss.

Some patients have small CDR but significant visual field loss, whereas some have large CDR with little visual field loss. Finally, while the CDR is of some value in patients with concentric cupping,[12] it may be seriously misleading when the loss of rim is limited to a single sector, as with a focal notch.

In this latter situation, the CDR may be recorded as small, and yet the disc and visual field may be badly damaged. The DDLS was designed to be reliable, user-friendly, and reproducible. Reliability of the DDLS has been assessed by Bayer and colleagues[13] who concluded that the DDLS correlated strongly with the amount of visual field damage. DDLS is a useful diagnostic parameter in glaucoma patients and was closely correlated to the perimetry, CDR, and OCT parameters.[14]

In our study, the average optic disc size was 1.85 mm ± 0.35 (range 1.30 mm to 2.8mm). Out of 104 eyes, 11 (10.6%) had small disc size <1.5 mm, 69 (66.3%) had average disc size with 1.5 to 2.0 mm and 24 (23.1%) had >2.0 mm disc size. In our study DDLS has low negative correlation with disc size (r = -.300, p = .002). Similar to our study Suresha AR [15] study showed average vertical disc size of 1.87mm ± 0.26. Eleven and half percent of the patients had disc size <1.5 mm, 57.5% of the patients had disc size with 1.5 to 2.0 mm and 31% of patients had more than 2.0 mm disc size. In a study by Chandra,[3] the average optic disc size was 2.03 mm ± 0.23. In the study by Kara Jose,[16] 85% had average size, 3% were small and 12% were large.

The most common DDLS stage was stage 4 (37.5%) followed by stage 5 (22.1%) according to the new DDLS stage. In our study, 9 (8.7%) eyes had DDLS stage 1-3, 62 (59.6%) eyes had DDLS stage 4-5, 15 (14.4%) eyes had stage 6-7, 14 (13.5%) had stage 8-9 and 4 (3.8%) had stage 10. DDLS showed low negative correlation with disc size (r = -.300, p = 0.002). In Kara Jose AC [16] study unlike our results, forty one eyes (41%) had DDLS > 5, sixteen (16%) eyes had DDLS > 7 and three (3%) had DDLS = 10.

The present study was carried out to determine the correlation between DDLS and VCDR with results of HFA in glaucoma patients. In our study, DDLS showed a coefficient correlation value of r = -.628, r = .391, r = .395 and r = -.278 (p= <0.000) when correlated against HFA MD, PSD, GHT and VF defect respectively. VCDR showed a coefficient correlation value of r = -.524, r = .317, r = .221and r = -.270 when correlated against HFA MD, PSD, GHT and VF defect respectively. DDLS has better correlation compared to VCDR with all the parameters.

In the study by Chandra,[3] they found a stronger correlation of DDLS with MD in VF (- 0.7958) than between CDR with M.D (- 0.708). The CDR does not take into consideration the optic disc size. Hence, large discs which are likely to have larger CDR (but may have normal neuro retinal rims) are more likely to be classified as glaucomatous while small CDR are more likely to be classified as normal when they actually have glaucoma. Bayer *et al*[13] study showed DDLS was strongly correlated with both MD (Pearson r = - 0.695, P < .001) and PSD (Pearson r = .703, *P* < .001). The HFA visual field staging system was also strongly correlated with the DDLS (Spearman r = .711, P < .001**).**

In the study by Suresha,[15] DDLS showed a coefficient correlation value of r = 0.81, r = - 0.80 and r = 0.46 (p<0.0001) when plotted against VFD, MD and PSD respectively. CDR showed a coefficient correlation value of r = 0.69, r = - 0.68, r = 0.27 when plotted against VFD, MD and PSD respectively. DDLS had an excellent predictability compared to CDR.

A significant negative correlation was observed between the DDLS stage and MD (r = - 0.267, p < 0.001) and a positive correlation was observed between the DDLS stage and visual field PSD (r = 0.233, p = 0.001) in the study done by Kitaoka.[17]

In the study by Maru,[18] DDLS correlated with visual field indices i.e. MD and PSD (p value< 0.001). Also, vertical CDR & DDLS staging correlated with Modified HFA staging which was statistically significant (p <0.001). Danesh Meyer[19] did a similar scatter plot relation between MD of the VF and DDLS (r = -0.62) which was statistically similar to our results. They found DDLS staging system to be superior to CDR as clinical approach to the optic disc evaluation. DDLS is an excellent method to distinguish between glaucoma and normal eyes and it outperformed CDR.

Similarly, in a study done by Narayan,[20] DDLS shows a strong negative correlation with MD in VF (- 0.725) than VCDR with MD (- 0.639). DDLS also show a strong positive correlation with PSD (0.643) when compared to VCDR with PSD (0.585).

Kara Jose *et al*[21] found a strong positive correlation between DDLS and CDR (r = 0.82, p<0.001) and weaker correlation between DDLS and VF MD (r = - 0.51, p <0.001). Pandey *et al*[22] found that DDLS correlates more closely with visual field indices and HFA staging system. It appears to be superior to CDR for disc evaluation.

So, this study concluded that DDLS shows moderate negative correlation with MD and low positive correlation with PSD and very low negative correlation with visual field defect in HFA when compared to vertical CDR. As r value of DDLS with MD is - 0.628 compared to CDR with MD which is - 0.524, both CDR and DDLS staging systems are moderately correlating with MD. But DDLS has better correlation compared to CDR with all the parameters. Initially only the recording of vertical CDR in glaucoma patients was done. By using DDLS now, recording of disc size and rim to disc ratio was also done as this is helpful in monitoring the progression of glaucoma.

The limitation of this study is that our results are derived from cross sectional study. Furthermore, longitudinal studies are needed with large sample size to overcome the limitation.

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