Original Article, Special Focus - Glaucoma

Assessment of optic disk by disk damage likelihood scale staging using slit-lamp biomicroscopy and optical coherence tomography in diagnosing primary open-angle glaucoma

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Purpose: The current study was aimed at assessment of optic disk by disk damage likelihood scale (DDLS) staging using slit-lamp biomicroscopy and optical coherence tomography (OCT) in diagnosing primary open-angle glaucoma (POAG) patients. **Methods:** This was a cross-sectional observational study of 106 POAG patients, which was conducted from April 2017 to April 2018. All patients underwent slit-lamp fundoscopy with a +78 D lens and high-definition (HD)-OCT, and the vertical cup disk ratios (VCDRs) were recorded. Disk size and neuroretinal rim assessment were done, and the disk was then staged using the recent version, which stages the optic nerve head (ONH) from 1 to 10 as read from the DDLS nomogram table. DDLS scores >5 indicate glaucomatous damage. Pearson coefficient was used to correlate the DDLS staging by slit-lamp biomicroscopy with best-corrected visual acuity (BCVA), intraocular pressure (IOP), disk size, and VCDR and VCDR, mean deviation, and DDLS staging by HD-OCT. **Results:** The mean age of the patients was 59.54 ± 6.61 years. The male: female ratio was 2:1. The mean IOP was 16.04 ± 1.97 mmHg, and BCVA was 0.72 ± 0.13 LogMAR units. The mean VCDR on 78 D slit-lamp biomicroscopy was 0.76 ± 0.09 (standard deviation [SD]) (range 0.1–0.77), whereas on HD-OCT, the mean VCDR was 0.81 ± 0.09 (SD) (range 0.07–0.81). The mean deviation on visual field testing in decibels was −14.43 ± 3.31 (SD). The correlation coefficient between DDLS staging by slit-lamp biomicroscopy and DDLS staging by HD-OCT parameters was $r = 0.96$. **Conclusion:** There is a positive correlation between the DDLS system of optic disk evaluation on slit-lamp biomicroscopy and most of the HD-OCT evaluation parameters.

Key words: Disk damage likelihood scale (DDLS), high-definition optical coherence tomography (HD-OCT), primary open-angle glaucoma (POAG), slit-lamp biomicroscopy, vertical cup disk ratio (VCDR)

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Glaucoma is a chronic progressive neuropathy of the optic nerve characterized by loss of retinal ganglion cells leading to structural damage. It manifests clinically as defects in the retinal nerve fiber layer (RNFL), loss of neuroretinal rim (NRR), and defects in visual field testing (VFT).[1] The progression of the disease may be checked by early detection and treatment. Patients with glaucoma often present late as they do not appreciate early, slowly progressive changes in their visual field.[2] Thus, screening the population at risk for glaucoma and educating patients diagnosed with glaucoma for regular follow-ups are imperative, as they might not be able to perceive minor changes in peripheral fields.[3] The diagnostic tests for glaucoma include measuring intraocular pressure (IOP), the VFT, and optic nerve head (ONH) examination. The VFT as an early diagnostic tool has limitations as defects in the visual field occur after significant ganglion cell loss has occurred.[4]

The early glaucomatous changes can be picked up on clinical evaluation. Ophthalmologists can distinguish them from normal variations, either by ophthalmoscopy or by using various investigational tools like perimetry, tomography, and so on. Armaly[5] and Armaly and Sayegh[6] introduced the cup to disk (CD) ratio as a standardized method to evaluate the ONH and communicate the ONH changes. Several studies have documented that larger CD ratios have more severe visual field changes on perimetry.[7-9] But the CD ratio neither directly describes the focal changes in the NRR nor considers the diameter of the optic disk, as small disks have fewer nerve fibers and smaller CD ratios than the larger disks. The focal rim loss of the disk at the vertical poles is characteristic of glaucoma.[9-14]

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Thus, looking for alternative investigation options that allow more reliable glaucomatous patients' determination is vital.

Also, there is high interobserver variability and low reproducibility in reporting clinical examination of the ONH changes. Some new methods for evaluating the ONH have been proposed to overcome these limitations.[15] Spaeth *et al*.[16] devised the disk damage likelihood scale (DDLS) to assess the disk size and the radial NRR width of the disk in clinical grading of the disk, which correlates strongly with the perimetry field changes having high interobserver reproducibility.[17-19]

The DDLS provides a more accurate assessment of optic disk damage than the conventional CD ratio measurement.[19] A strong correlation has been found between the DDLS and various indices obtained from optical coherence tomography (OCT) in patients with primary open-angle glaucoma (POAG).[20,21]

Though one can rely on imaging devices for glaucoma diagnosis, they are expensive and continuously evolving, limiting their availability and usefulness.[22-26] Therefore, the DDLS assessed by slit lamp can be used in various clinical settings at low cost and in a setting with scarce resources.

This study correlates the diagnostic accuracy of the DDLS staging assessed by slit-lamp biomicroscopy performed during clinical examination and the DDLS grading on high-density optical coherence tomography (HD-OCT) imaging parameters. To the best of our knowledge, this is the first study in northern India correlating the DDLS staging by slit-lamp biomicroscopy to that with HD-OCT parameters.

Methods

This cross-sectional observational study was conducted over 1 year, from April 2017 to April 2018, at a tertiary eye care referral center in northern India. The study followed the tenets of the Declaration of Helsinki, and study approval was obtained from the Institutional Ethics Committee (IEC)

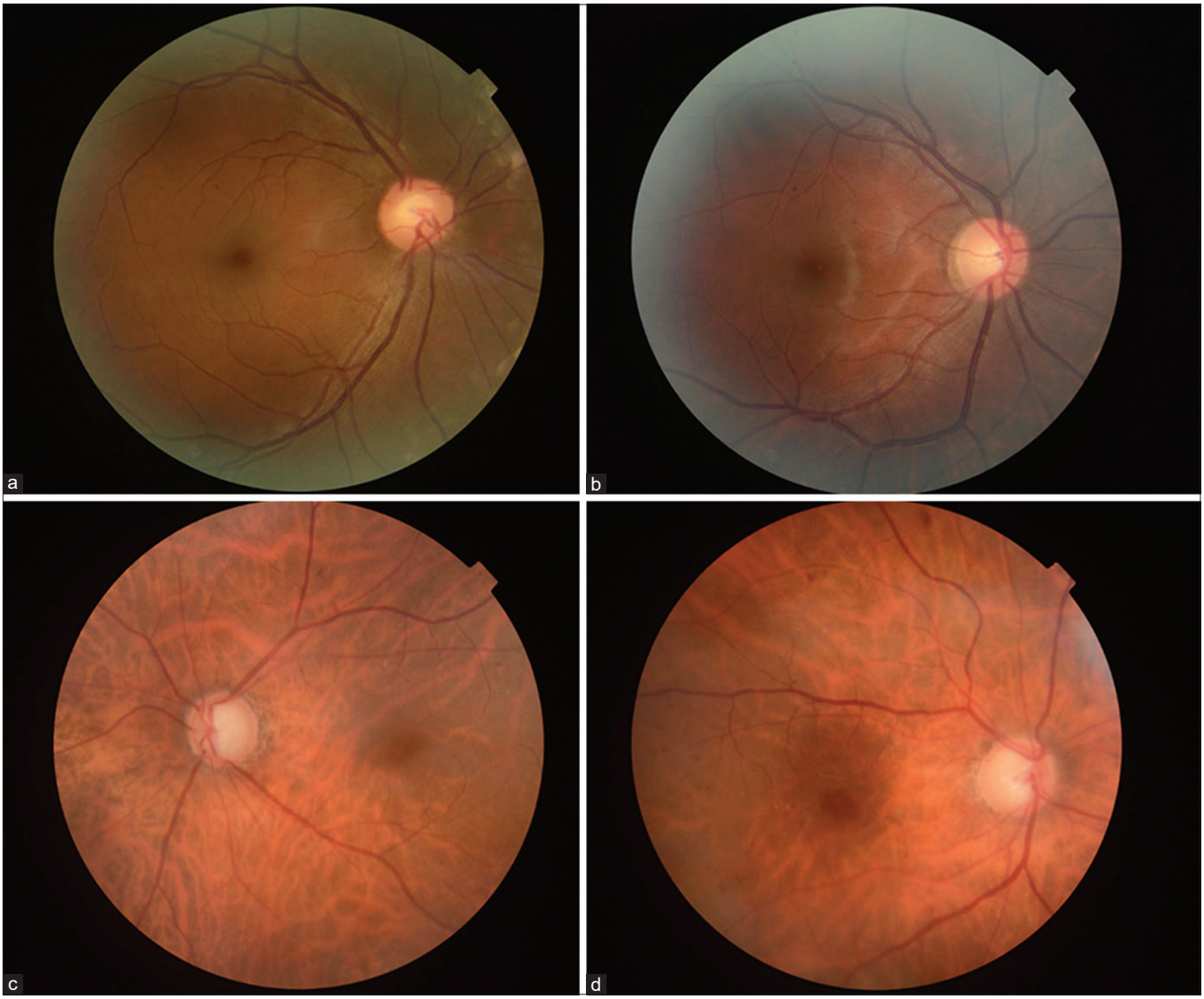

Figure 1: (a) Digital fundus image of the patient's right eye depicting normal fundus with a DDLS score of 2. (b) Digital fundus image of the patient's right eye depicting fundus image of disk at risk with a DDLS score of 3. (c) Digital fundus image of the patient's left eye depicting fundus image of disk with a DDLS score of 8. (d) Digital fundus image of the patient's right eye depicting fundus image of disk with a DDLS score of 8. DDLS = disk disease likelihood scale

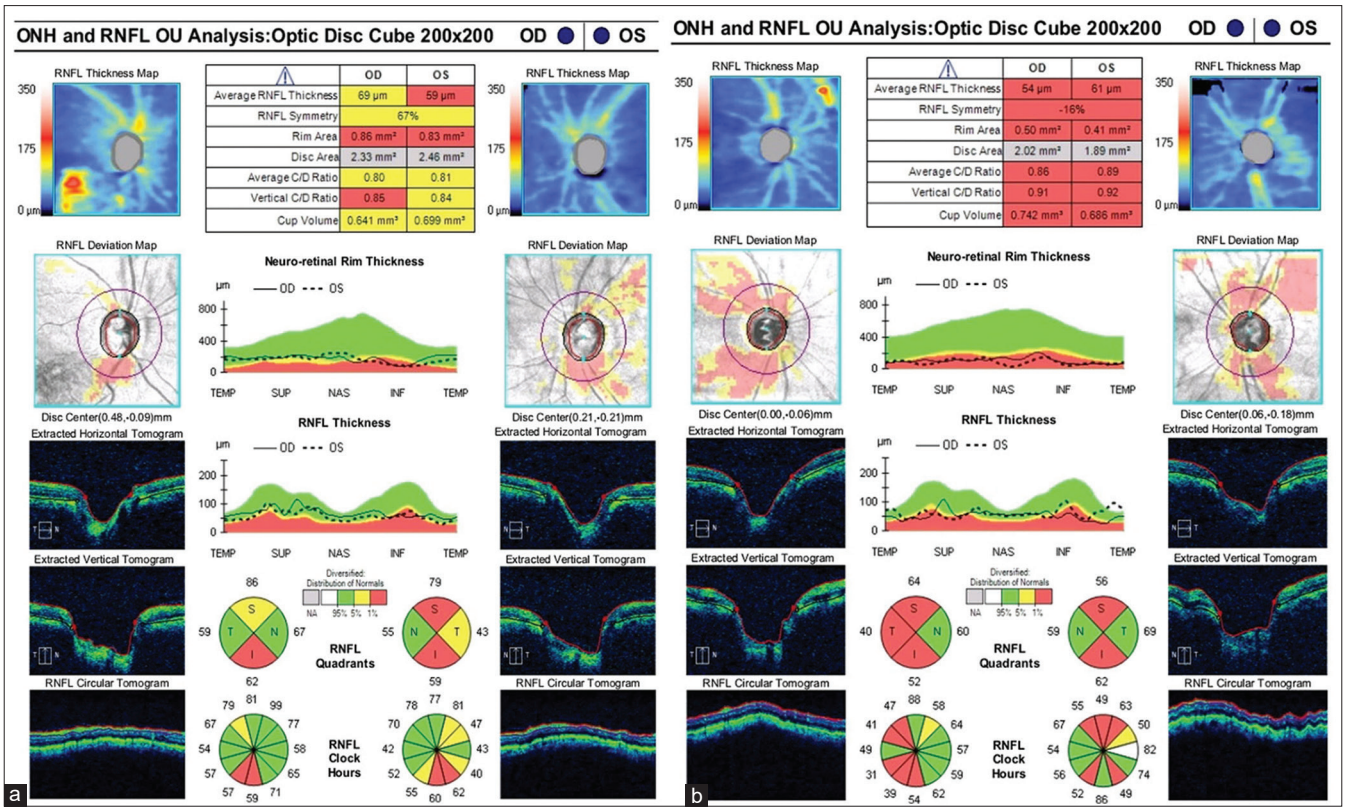

Figure 2: (a and b) Digital HD-OCT scan of the ONH and RNFL depicting bilateral glaucoma cupping with corresponding RNFL thinned-out area seen as red plots. HD-OCT = high-definition optical coherence tomography, ONH = optic nerve head, RNFL = retinal nerve fiber layer

of the Institutional Review Board (IRB). Informed consent was taken from all the patients. Prediagnosed POAG patients were enrolled at our glaucoma clinic during the study period. POAG was diagnosed based on the International Society for Geographical and Epidemiological Ophthalmology (ISGEO) classification.[25] One hundred and six POAG patients were recruited from the specialty clinic. Only one eye of each patient with better reliability indices was included in the study. The inclusion criteria were prediagnosed cases of POAG based on increased IOP, fundoscopy findings, open angles on gonioscopy, with a best-corrected visual acuity (BCVA) of 6/60 or better on Snellen's chart, spherical refraction within ±5.0 D and cylinder correction within ±3.0 D, reliable automated perimetry following Anderson's criteria, and signal strength more than six on Spectral Domain Optical Coherence Tomography (SD-OCT). The exclusion criteria were the presence of ocular media opacities that interfere with the examination; anterior segment abnormalities (except the alterations caused by uncomplicated glaucoma or cataract surgery); the presence of other intraocular or neurological diseases affecting the RNFL, optic disk, or the visual field; and abnormal appearance of ONH, such as tilted disk, nonglaucomatous disk damage, or extensive peripapillary atrophy. Other exclusion criteria included history of intraocular trauma and surgery (except uncomplicated cataract or glaucoma surgery at least 6 months before examinations), subjects <25 years of age, and inability to perform reliable perimetry (defined as false-positive rate <20%, fixation loss <20%, and false-negative rate <20%, with no visual field artifacts).

Table 1: Demographics of study patients (*n*=106)

Parameter	Value
Age	
Mean age (SD)	59.54 (±6.61)
Gender	
Male	67 (63.21%)
Female	39 (36.79%)
Refractive error	
Myopic	79 (74.52%)
Hypermetropic	27 (25.47%)
Mean intraocular pressure (SD)	16.04 (±1.97)
Mean best-corrected visual acuity (SD)	0.72 (±0.13)
Mean vertical cup to disk ratio on slit-lamp biomicroscopy (SD)	0.76 (±0.09)
Range	0.1-0.77
Mean vertical cup to disk ratio on HD-OCT (SD)	0.81 (±0.09)
Range	0.07-0.81
Mean deviation (dB) on visual field testing (SD)	−14.43 (±3.31)

HD-OCT=High-definition optical coherence tomography, SD=Standard deviation

All subjects underwent a comprehensive ophthalmological examination. Detailed medical history, subjective refraction, Snellen's BCVA, slit-lamp biomicroscopy (Haag Streit AG, Koniz, Switzerland), IOP by Goldmann applanation tonometry (GAT), gonioscopy, and dilated fundus biomicroscopy with +78 D lens and HD-OCT with Cirrus HD-OCT 500 (Carl Zeiss Meditec AG Goeschwitzer Str. 51-52

07745 Jena Germany) were evaluated and recorded for all the subjects.

The abnormal glaucomatous visual field changes along with glaucomatous optic neuropathy in the form of asymmetry between fellow eyes of greater than 0.2, excavation, rim thinning, notching, or RNFL defects defined the glaucomatous eye. For DDLS grading, eyes were examined by two glaucoma specialists using a volk 78 D noncontact lens on slit-lamp biomicroscopy (Haag Streit AG), who were blinded to the OCT results at the time of reporting. The graticule size in millimeters was multiplied by 1.1 as a correction factor for the lens.[1,27] The measurement of disk size and assessment of NRR were done, and the disk was then staged using the recent version, which stages the ONH from 1 to 10 as read from the DDLS nomogram table. DDLS scores >5 indicate glaucomatous damage[1,20] [Fig. 1]. HD-OCT imaging was performed with Cirrus HD-OCT 500 (Carl Zeiss Meditec, Inc.) on dilated pupils of the patients by two experienced examiners [Fig. 2]. Pearson's correlation coefficient was used to correlate the parameters observed on slit lamp biomicroscopy and parameters observed on HD-OCT.

Table 2: DDLS staging by slit-lamp biomicroscopy parameters

DDLS staging	Disk size (*n*, %)		
	Large disk (>2 mm)	Medium disk (1.5-2 mm)	Small disk (<1.5 mm)
5	5 (4.7%)	7 (6.6%)	0 (0.0%)
6	8 (7.5%)	10 (9.4%)	1 (0.9%)
7	10 (9.4%)	15 (14.2%)	1 (0.9%)
8	11 (10.4%)	15 (14.2%)	0 (0.0%)
9	3 (2.8%)	12 (11.3%)	0 (0.0%)
10	0 (0.0%)	6 (5.7%)	2 (1.9%)

DDLS=disk damage likelihood scale

Table 3: DDLS staging by HD-OCT parameters

DDLS staging	Disk size (*n*, %)		
	Large disk (>2 mm)	Medium disk (1.5-2 mm)	Small disk (<1.5 mm)
5	0 (0.0%)	6 (5.7%)	0 (0.0%)
6	7 (6.6%)	11 (10.4%)	1 (0.9%)
7	11 (10.4%)	15 (14.2%)	1 (0.9%)
8	13 (12.3%)	15 (14.2%)	0 (0.0%)
9	4 (3.8%)	12 (11.3%)	0 (0.0%)
10	2 (1.9%)	6 (5.7%)	2 (1.9%)

DDLS=disk damage likelihood scale, HD-OCT=high-definition optical coherence tomography

Table 4: Pearson correlation coefficient test between DDLS staging by slit-lamp biomicroscopy and other parameters

Parameters	*r*	*P*
DDLS versus BCVA	0.541**	<0.001
DDLS versus IOP	0.124	0.204
DDLS versus disk size	−0.017	0.865
DDLS versus VCDR 78 D	0.562**	<0.001
DDLS versus VCDR OCT	0.606**	<0.001
DDLS versus DDLS OCT	0.958**	<0.001
DDLS versus MD	−0.707**	<0.001
DDLS versus average RNFL	−0.747	<0.001

BCVA=Best-corrected visual acuity, DDLS=Disk damage likelihood scale, IOP=Intraocular pressure, MD=Mean deviation, OCT=Optical coherence tomography, RNFL=Retinal nerve fiber layer, VCDR=vertical cup disk ratio. **Statistically significant with a *P*<0.05

Statistical analysis

Statistical data analysis was done using Statistical Package for the Social Sciences (SPSS) software (version 23.0; SPSS Inc., Chicago, IL, USA). Data were summarized as mean and standard deviation (SD) for numerical variables and count and percentage for categorical variables. Pearson's correlation coefficient was used to correlate two continuous variables. *P* value <0.05 was considered statistically significant.

Results

We analyzed a total of 106 POAG patients. There were 67 males (63.2%) and 39 females (36.8%). The male: female ratio was 2:1. The mean age of patients was 59.54 ± 6.61 (SD) years. The majority of patients were in the 51–60 years age group (62, 58.5%), followed by 61–70 years age group (38, 35.8%). The mean Snellen's BCVA was 0.72 ± 0.13 (SD) LogMAR units, and the mean IOP was 16.04 ± 1.97 (SD) mmHg. Seventy-nine (74.5%) patients were myopic, and 27 (25.5%) were hypermetropic. The mean VCDR on + 78 D slit-lamp biomicroscopy was 0.76 ± 0.09 (SD) (range 0.1–0.77), whereas on HD-OCT, the mean VCDR was 0.81 ± 0.09 (SD) (range 0.07–0.81). The MD on VFT in decibels was − 14.43 ± 3.31 (SD) [Table 1].

DDLS staging for each patient was done based on the parameters collected by slit-lamp biomicroscopy and the parameters collected by HD-OCT [Figs. 1 and 2]. We found that most of the study patients had DDLS stage 7 or 8 based on the assessment by both the techniques [Figs. 1 and 2]. The details of these are presented in Tables 2 and 3. A positive correlation was found between DDLS staging by biomicroscopy and BCVA (r = 0.54), VCDR of slit-lamp biomicroscopy (r = 0.56), and VCDR of HD-OCT (r = 0.61). Also, there was an inverse correlation between DDLS staging by slit-lamp biomicroscopy and MD (r = −0.71). There was a strong positive correlation between DDLS staging by slit-lamp biomicroscopy and DDLS staging by HD-OCT parameters (r = 0.96) [Table 4].

Discussion

Although the most commonly used method to evaluate disk changes is the CD ratio method proposed by Armaly *et al*.,[6] it has several limitations. Later, in 2002, Bayer *et al*.[17] devised DDLS scoring, overcoming the VCDR method's limitations. The purpose of our study was to compare the DDLS scale staging by slit-lamp biomicroscopy and by OCT in patients with POAG. Further, we also analyzed the correlation of DDLS with the conventional VCDR method. Further correlations between VCDR and MD, DDLS with MD, and DDLS and RNFL were also studied. We believe this is the first study doing neck-to-neck comparison between all these parameters.

Meyer *et al*.,[20] in a comparative analysis of the relationship between global indices of Humphrey standard automated

perimetry (SAP; 30-2 SITA standard test), Humphrey matrix frequency doubling technology (FDT; 30-2 threshold test), and Heidelberg retina tomograph (HRT II) parameters among glaucoma patients reported a mean age of 58 years.. This shows the average age of diagnosed cases of glaucoma is around 58–60 years, which is similar to our results.

We found the MD on visual fields to be −14.43 D (SD 3.31 D). This is in contrast to the study findings of Danesh-Meyer HV *et al*.,[20] who reported a much lower MD on Humphrey visual field assessment using SITA-standard as −4.95 D (SD 5 D).[28] This might be because exclusively POAG-diagnosed patients were included in our study compared to normal, diagnosed, and suspect cases in the study by Meyer *et al*.[20]

We studied the correlation of VCDR with DDLS scoring using Pearson's coefficient (*r*) and found a highly significant positive correlation between these two parameters. We found that evaluation of DDLS versus VCDR with a +78 D lens showed a strong correlation with an *R*-value of 0.562 and a *P* value of <0.001. Also, we compared the DDLS scoring with VCDR based on OCT and again found a strong correlation with an *R*-value of 0.606 and a *P* value of <0.001. Kara-Jose *et al*.,[29] in their study, also compared DDLS correlation with vertical and horizontal Cup disc ratio (CDR). They also found a strong correlation of DDLS with vertical (r = 0.79) and horizontal (r = 0.74) C/D ratios and with the parameters VCDR and C/D area ratio from OCT (0.75 and 0.72, respectively).[30]

When we compared the correlation of VCDR with MD, RNFL VS DDLS with MD, and RNFL, we found no significant difference for any of the three parameters. These findings correlate with the study findings of Chandra *et al*.,[28] who reported no significant difference for mean deviation (MD) and pattern standard deviation (PSD). Still, they found a considerable difference in RNFL thickness. They found a stronger correlation of DDLS with MD in visual field testing (VF) (−0.7958), similar to our study ($\boldsymbol{r}$ = −0.635), and between C/D ratio and MD (−0.708), which was again similar to our study ($\boldsymbol{r}$ = −0.698). However, the correlation of DDLS with PSD was 0.45896 and that of VCDR with PSD was 0.49484, which were weaker than the values obtained in our study (r = 0.647, r = 0.703, respectively). Similarly, the correlation of DDLS with RNFL thickness was −0.8472 greater than our study value (r = −0.680). We compared our study results with theirs and found that VCDR correlated better with the functional test parameters than DDLS. Similarly, in another study by Kara-José *et al*.,[29] a robust positive correlation was found between DDLS and CDR (Spearman r = 0.82; P < 0.001).

The VCDR method of evaluating glaucomatous disk has its limitations of observer bias. In this method, the disk size is not considered. Hence, large disks are more likely to be classified as glaucomatous, while small disks with smaller vertical CD ratio (VCDR) are more likely to be considered normal, although they can be glaucomatous. In comparison, the DDLS staging has advantages such as it takes into account the disk size, focuses on NRR tissue thinning, and considers the thinnest part of the rim for calculation.

The limitations of DDLS include the following: DDLS can remain static even with continuing damage, as it considers the thinnest rim width. So, whether it is a focal thinning of the disk or generalized atrophy, DDLS scoring remains the same in these cases. Hence, there is a need for constant follow-up of the patient and taking the help of other modalities to assess the damage better and allow objective comparison at every visit with the previous one. Moreover, it also requires skill to learn, so the learning curve is longer for the usage of DDLS.

We further correlated the diagnostic accuracy of slit-lamp biomicroscopy staging of DDLS with VCDR, MD, and DDLS staging by HD-OCT parameters. DDLS had significant moderate to strong correlations with most structural and functional measurements. It was positively correlated with VCDR (r = 0.56 for slit lamp and r = 0.61 for HD-OCT; P < 0.001). The study of Majid *et al*.[30] also reported VCDR (0.59) on Stratus OCT as one of the parameters moderately correlated with DDLS. Similarly, Han *et al*.[31] also reported strong correlations between DDLS and VCDR (0.74) on Cirrus OCT. The few limitations of our study include that the sample was collected from among prediagnosed cases of POAG, and the extent of damage, previous treatment, and control of IOP at the time of inclusion of subjects into the study were not correlated with the parameters tested. Further, patients with ONH rim thinning were not excluded from the evaluation, since ONH assessment, especially the NRR, is part of the DDLS system and could result in an overestimation of the DDLS correlations.

Conclusion

To conclude, we found that VCDR correlated slightly better with MD and PSD, which are functional test parameters, than DDLS. DDLS was found to have a strong negative correlation with RNFL compared to VCDR, which is a structural test parameter. So, in the early diagnosis of glaucoma, DDLS will be more helpful than the conventional VCDR method. The results also showed significant accuracy and correlation of the DDLS system of optic disk evaluation on slit-lamp biomicroscopy with most of the parameters of HD-OCT evaluation. We assume that the results of this study will be beneficial in enhancing ophthalmologists' understanding and standardizing the cup disk ratio findings by reducing interobserver variations among different ophthalmologists.

Compliance with ethical standards

The article complies with the ethical standards of the Declaration of Helsinki.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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