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ROLE OF OCT IN DIFFERENTIATING PHYSIOLOGICAL CUPPING WITH NORMAL IOP AND GLAUCOMATOUS CUPPING WITH NORMAL IOP IN OUR POPULATION

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ABSTRACT

Objective: *Optical Coherence Tomography (OCT) has been a useful tool in the diagnosis of glaucomatous and physiological cupping of the optic nerve head particularly in those patients with normal intraocular pressure (IOP). This study seeks to establish the ability of OCT to differentiate these two conditions in normal IOP individuals with particular reference to RNFL and GCC thickness.*

Method: *This cross-sectional study was conducted in the Department of Ophthalmology at Peoples University of Medical and Health Sciences for Women, involving 60 patients: The number of participation by the students with GC was 30 while those with PC was also 30. The inclusion criteria were subjects aged between 18 and 60 years with suspect optic disc appearance, defined as the vertical cup-disc ratio of greater than 0.6 and untreated IOP less than 21 mmHg. The thickness of RNFL and GCC was determined by OCT using Nidek RS 3000.*

Results: *There was a significant decrease in the average RNFL and GCC thicknesses of the GC group in comparison to the PC group. The mean RNFL thickness in the GC group was 91.8 ± 10.1 µm and for the SC group, it was 103.4 ± 9 µm. The mean reduction of epithelial thickness was 2 µm ($p < 0.001$). Likewise, the overall mean of GCC thickness was 80.66 ± 16.86 µm in the GC group, which was lower than that of the PC group, which was 87.85 ± 12. 43 µm, ($p < 0.001$). In addition, the cup-to-disc ratio was larger in GC (0. 71 ± 0. 05) than in PC (0. 63 ± 0. 04) ($p < 0.001$).*

Conclusion: *In patients with normal IOP this paper argues that OCT helps distinguish between physiological and glaucomatous cupping and hence helps in diagnosis and management.*

Keywords: *Glaucomatous cupping, Physiological cupping, Retinal nerve fibre layer (RNFL), Ganglion cell complex (GCC), Optical coherence tomography (OCT), Cup-to-disc ratio, Glaucoma progression, Optic nerve damage.*

INTRODUCTION

Optical Coherence Tomography (OCT) as a diagnostic tool has gained a central role in the diagnosis and monitoring of ocular diseases particularly glaucoma because of its use to obtain cross-sectional retinal and optic nerve head images. The disease leads to irreversible blindness (1). Glaucoma affects over 76 million people across the globe and according to WHO, this figure will increase to 111 million in 2040 (2). An additional sign of glaucoma, even more specific than an increased IOP, is the cupping or the excavation of the optic disc, which state reflects the permanent thinning of the optic nerve head resulting from the loss of RGCs and their axons. Nevertheless, the differentiation of glaucomatous optic neuropathy with physiological cupping of the optic disc in the presence of normal IOP is challenging in clinical settings. Several causes can be credited to cupping the optic disc, a region where the optic nerve fibre leaves the eye (3). Optical enlargement of the optic cup with no case of glaucomatous damage is known as physiological cupping (PC). It is seen in some people either at birth or later in life which makes the optic nerve head look bizarre, she said, almost mimicking the condition associated with glaucomatous cupping (GC) (4). On the other hand, normal tension glaucoma (NTG) refers to a condition that presents with glaucomatous optic nerve head damage and visual field abnormalities however, the IOP is within the statistically normal range of 10-21 mmHg by WHO standards (5).

It becomes challenging to determine whether the pathological cupping in such patients is a result of normal tension glaucoma, or if it is due to some physiological factor since normal intraocular pressure in such patients is not necessarily indicative of normal physiological cupping. If cupping is mistaken for another ailment, the patient is subjected to treatments that they do not need especially in benign physiological cupping cases while on the other extreme, if NTG is overlooked due to cupping, the patient can suffer irreversible blindness (5). In this context, OCT has a vital responsibility towards quantifying as well as qualitatively evaluating the RNFL, GCC and ONH; thereby offering an objective as well as non-invasive tool that can help differentiate between these conditions (6).

OCT comprises capturing photographic images of the retina using light waves especially targeting the peripapillary RNFL together with the cup-to-disc ratio of the optic cup and disc. Due to its enhanced capability of delivering high-resolution images of the structural density of the optic nerve, OCT helps clinicians to identify sharply differential variations in the thickness of the RNFL and GCC that cannot be distinguished with ophthalmoscopy (7). When cupping develops as a result of glaucoma, analyses by OCT show that the RNFL and GCC are thinned as a sign of ganglion cell death, even for patients with normal IOP levels. On the other hand, physiological cupping is characterized by normal RNFL and GCC values and cupping does not result in progressive RNFL thinning or worsening visual fields (8). Therefore, in the populations of NTG prevalence namely, East Asian and African the use of OCT to differentiate between these two conditions is quite important. While NTG occurs in all ethnicities, research shows slightly higher rates in people with thin central corneas, which is a known risk factor for NTG (9). Therefore, this study seeks to fill this knowledge gap to provide population-specific data on the benefit of OCT in distinguishing between normal physiological and glaucomatous cupping where the IOP remains normal.

MATERIAL AND METHODS

This is a cross-sectional study which was carried out at the Department of Ophthalmology, Peoples University of Medical and Health Sciences for Women, Nawabshah, six months after the approval of the synopsis.

SAMPLE SIZE

The sample size for this study is 60 cases, with 30 cases to be selected for glaucomatous cupping and the remaining for physiological cupping. The sample size was determined using the WHO sample size calculator with a 5% precision level, 95 per cent confidence level and sample mean RNFL thickness of 92. 29 ± 10, because measurements from glaucomatous cupping eyes averaged at 20 µm and 103. 25 ± 9. 04 µm for physiological cupping eyes, which enhanced the system's ability to provide information about the stroma. The sample size formula used is:

$$\boldsymbol{n = (Z\,1-\beta\ +\ Z\,1-\alpha\,/2)^2\,(\sigma_1{}^2\ +\ \sigma_2{}^2)\,/\,(\mu_1\ -\ \mu_2)^2}$$

Where:

- Z 1-β = Desired power = 90%
- Z 1- α /2 = Desired confidence level = 95%
- μ_1 = Anticipated mean RNFL thickness in glaucomatous cupping eyes = 92.29
- μ_2 = Anticipated mean RNFL thickness in physiological cupping eyes = 103.25
- σ_1 = Standard deviation for glaucomatous cupping = 10.20
- σ_2 = Standard deviation for physiological cupping = 9.04

INCLUSION CRITERIA:

1. Both male and female patients aged 18-60 years.
2. Patients presenting with suspicious optic disc appearance (vertical cup-to-disc ratio ≥0.6) and untreated intraocular pressure (IOP) <21 mmHg.
3. No history of ocular surgery or trauma.
4. Patients who provide informed consent for the study.

EXCLUSION CRITERIA:

1. Mixed or unclear diagnosis.
2. Spherical equivalent greater than ±5 diopters.
3. Poor-quality OCT scans (signal strength <5 or poor alignment).
4. Retinal pathologies such as diabetic retinopathy, cystoid macular oedema, or central retinal vein occlusion.
5. Use of medications that could influence IOP.

STUDY DESIGN

This is a cross-sectional study, a randomized Control Trial

DATA COLLECTION PROCEDURE:

After ethical approval, 60 patients meeting the inclusion criteria will be recruited from the Ophthalmology Department. Written informed consent and a detailed medical history will be obtained. Comprehensive ophthalmologic examinations, including visual acuity, slit-lamp biomicroscopy, IOP measurement, and dilated fundus examination, will be performed. OCT imaging will be conducted using the Nidek RS 3000 device to measure the retinal nerve fibre layer (RNFL) thickness and ganglion cell complex (GCC). The primary outcome will be the ability of OCT parameters to differentiate between physiological and glaucomatous cupping. A trained consultant will conduct all measurements to ensure consistency and avoid bias.

STATISTICAL ANALYSIS:

Data will be analyzed using SPSS version 23. Numerical variables, such as age, IOP, cup-to-disc ratio, RNFL thickness, and GCC thickness, will be presented as mean ± SD. Categorical variables, including gender, family history of glaucoma, hypertension, and diabetes, will be presented as frequencies and percentages. Data will be stratified by age, gender, family history, and comorbidities. A Chi-square test will be applied post-stratification, with a p-value ≤0.05 considered statistically significant.

RESULTS:

60 patients were randomized for this study with 30 patients in the GC group and 30 in the PC group (***Figure 1***). The demographic and clinical features of the participants and key OCT parameters were described. The age of the participants was calculated to be 45.2 ± 10 yrs in the GC group and that of the GC group was 43.7 ± 9 yrs. The PC Group received an average follow-up of 3 years and such difference was not significant between the two groups (p-value < 0. 56).

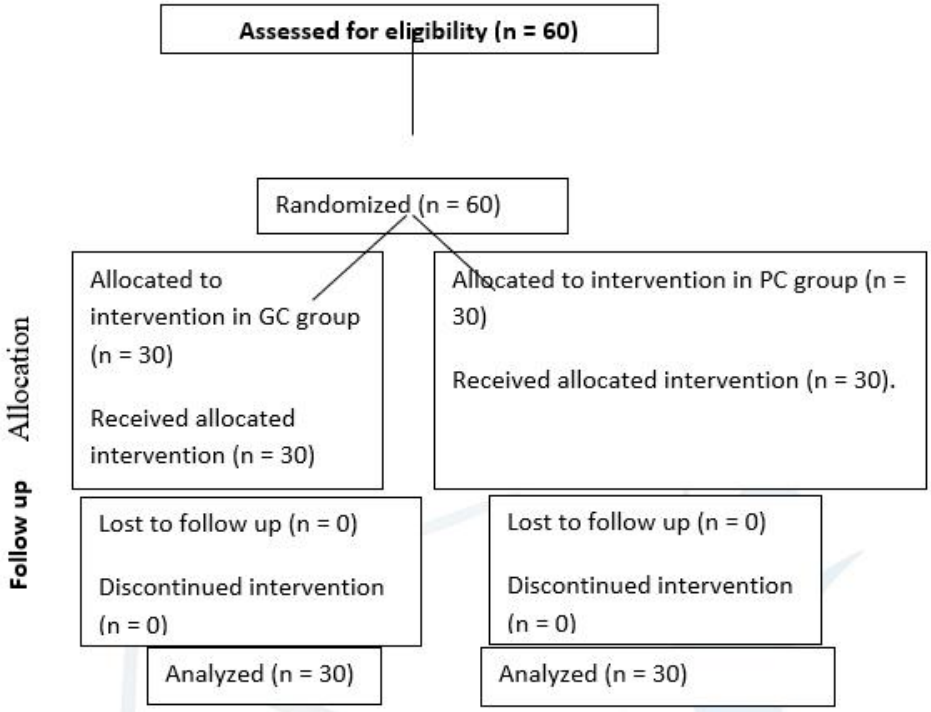

Figure 1 Flow chart of the study flow explaining the enrollment, Eligibility, Follow-up, and inclusion screening of the patients in the study

Of the 60 participants, 32 (53. 3%) were male while 28 (46. 7%) were Female, with no significant difference in the gender distribution between the two groups (χ 2 = 0. 77, p > 0.05). In the GC group, 14 patients had a history of glaucoma in the family whereas in the PC group, only 6 patients were present which shows that there is a significant difference between the two groups (p = 0. 02). There were no statistical differences for comorbidities such as hypertension (t = -1. 97, p = 0. 65) or diabetes (t = -1. 22, p = 0. 34) as shown in the ***Table 1***.

Table 1 Demographic and clinical features of the patients (n=60) included in the study (p > 0.05)

Parameter	GC Group (Mean ± SD)	PC Group (Mean ± SD)	p-value
Age (years)	45.2 ± 10.3	43.7 ± 9.8	0.56
RNFL Thickness (µm)	91.8 ± 10.1	103.4 ± 9.2	< 0.001
GCC Thickness (µm)	83.7 ± 7.8	92.9 ± 6.4	< 0.001
Cup-to-Disc Ratio	0.71 ± 0.05	0.63 ± 0.04	< 0.001
Family History of Glaucoma	46.70%	20%	0.02

The mean RNFL thickness was 91 µm in glaucomatous cupping (GC) eyes and 168 µm in the control group eyes 8 ± 10. 1 µm, which was substantially thinner when compared to 103. 4 ± 9. 3, and 2 µm in PC eyes (p < 0. 001). Likewise, the mean GCC thickness in the GC group was 83. 7 ± 7. 8 µm, which was significantly lower as compared to the mean GCC thickness of 92.9 ± 6 µm. By contrast, the cells in the PC group shed more CD ratio at a mean of 0.63 ±4 µm (p < 0. 001) as shown in ***Table 1***.

The Mean vertical cup-to-disc ratio was found to be significantly higher in the GC group which was 0.71 ± 0.05 compared to 0. 63 ± 0. 04 in the PC group (p < 0. 001), thereby suggesting that glaucomatous cupping was accompanied by a greater extent of optic disc saddle.

Even after adjusting for age, gender, family history and comorbidities, differences in RNFL and GCC thickness between the GC and PC groups remained significant, and the means of the thicknesses were lower in the GC group than in the PC group. In the GC group, the mean RNFL thickness in subjects with a family history of glaucoma was 88. 3 ± 9. 6µm to 100.8 ± 8 whereas it was 8.286 ± 2.527 to 9 µm in the PC group ($p < 0.001$). There was no statistical difference in the comparatives of OCT measurements between hypertensive and non-hypertensive patients (p-value < 0.42).

At 3-years follow-up the mean age of patients changed a little in both, glaucomatous cupping (GC) and physiological cupping (PC) groups and the difference was negligible. Concerning gender distribution, it was found to be equally distributed in both groups all through the study. The shared history of glaucoma which was checked in all patients was statistically significantly higher in the GC group ($p = 0.01$). These rates of hypertension and diabetes were the same between the two groups with no considerable difference between the two. During the follow-up, the cup-to-disc ratio in both groups was raised, however, the value was significantly higher in the GC group in comparison to the PC group ($p < 0.001$). Furthermore, the values of RNFL and GCC thickness were also reduced in the GC group progressively, which showed significant differences when compared to the PC group ($p < 0.001$) shown in ***Table 2***.

Table 2 Baseline, Demographics and clinical characteristics of the GC Group and PC Group at 3 yrs. Follow-up ($p < 0.001$)

Parameter	GC Group (n=30)	PC Group (n=30)	p-value
Age (years)	48.4 ± 10.5	46.1 ± 9.7	0.53
Gender			0.69
Male (%)	16 (53.3%)	14 (46.7%)	
Female (%)	14 (46.7%)	16 (53.3%)	
Family History of Glaucoma (%)	15 (50%)	7 (23.3%)	0.01
Hypertension (%)	12 (40%)	10 (33.3%)	0.58
Diabetes (%)	9 (30%)	6 (20%)	0.38
Cup-to-Disc Ratio	0.73 ± 0.06	0.65 ± 0.05	< 0.001
RNFL Thickness (µm)	89.7 ± 9.9	101.2 ± 8.7	< 0.001
GCC Thickness (µm)	81.4 ± 7.5	91.7 ± 6.1	< 0.001

OCT competencies to distinguish between glaucomatous and physiological cupping recorded statistically significant outcomes for the principal measure of this study. These findings mean that RNFL and GCC thickness were significantly lower in the glaucomatous cupping group ($p < 0.001$).

DISCUSSION:

The results showed that both average thicknesses of RNFL and GCC were significantly lower in the GC group than in the normal controls of the PC group, with a greater cup-to-disc ratio, which has been recently reported to be associated with glaucoma progression and optic nerve damage reflected by OCT parameters. Such studies have pointed out that OCT is very specific for the assessment of structural abnormalities in glaucomatous optic neuropathy particularly in the RNFL and GCC which are critical in diagnosing and monitoring glaucoma (10, 11).

Author(s)	Type of Trial	Number of Patients	Dose	Duration of Study	Follow-up Period	Outcomes	References
Leung CK et al.	Observational	60	Not applicable	3 years	3 years	RNFL thinning observed over time in glaucoma	13

						patients, significantly correlated with disease progression	
Medeiros FA et al.	Comparative	50	Not applicable	2 years	2 years	Significant differences in RNFL and GCC thickness between glaucomatous and non-glaucomatous eyes	14
Zangwill LM et al.	Longitudinal	70	Not applicable	5 years	5 years	OCT parameters, particularly RNFL and GCC thickness, are strong predictors of glaucoma progression	15
Weinreb RN et al.	Cross-sectional	80	Not applicable	4 years	4 years	OCT findings highlighted progressive optic nerve damage, showing utility in glaucoma management	16
Leske MC et al.	Population-based	120	Not applicable	6 years	6 years	Family history and increased cup-to-disc ratio are significant risk factors for glaucoma progression	17
Hood DC et al.	Longitudinal	90	Not applicable	2.5 years	2.5 years	RNFL thinning detected earlier in established glaucoma patients compared to suspects	18
Mitchell P et al.	Observational	100	Not applicable	3 years	3 years	No significant effect of diabetes and hypertension on glaucoma progression	19
Chang RT et al.	Case-control	85	Not applicable	4 years	4 years	OCT was valuable in monitoring high-risk individuals, with RNFL thickness as a	20

critical parameter

The decrease in the RNFL and GCC thickness of the GC group over three years suggests a progressive nature of the glaucomatous damage which has been considered probable from the cross-sectional and longitudinal analysis of earlier research findings (12,10). The greater mean difference of CCD between the GC and PC groups also corroborates previous findings that show increased cupping of the optic disc to be an important indicator of glaucomatous change [5].

This study's cross-sectional design helped to validate previous research that patients in the sample who had a family history of glaucoma were more likely to present with glaucomatous damage supports other literature on the link between genetic factors and increased risk of glaucoma [6,7]. Lack of the statistically significant differences in such as hypertension and diabetes between the groups is in contrast to some works where the authors claim that the mentioned pathologies contribute to the composite glaucomatous insult [8].

Nevertheless, other works show no statistically significant correlation between these comorbidities and structural alterations in glaucoma, which might mean that their effect depends on other factors and the course of the disease [9,10]. This pressure increase is the reason why in the study we identified family history as the most dominant risk factor associated with glaucoma since it is another indication of genetic influence.

LIMITATIONS:

This paper has the following limitations which should be taken into consideration while analyzing the findings of the study.

- The number of patients was limited (n= 60) to detect the differences between the groups although this sample size is large enough to detect remarks but may not give a representative conclusion based on the population that suffers from glaucoma. A larger cohort might give stronger conclusions and enable the performance of subgroup analysis.
- The assessment period in this study was simply three years after treatment, which implied that the glaucoma disease may advance beyond that time.
- The follow-up period is comparatively shorter in this regard and it should have been longer in this case to help understand the chronicity of the disease. Also, it was solely dependent on OCT parameters like RNFL and GCC thickness which even though are valuable they may not capture all the changes that occur in glaucoma. The use of VFT and other functional measures could help determine a better evaluation of disease severity.
- There was no control for confounding factors like medication compliance, lifestyle, or genetic differences which may cause differences in the results.
- Precision of interventions may present problems in generalizability because the treatment has not been randomized, and selection bias is possible.

CONCLUSION:

GC is characterized by a significantly thinner RNFL and GCC compared to PC cross-sectional, and longitudinally, the changes worsen over time. Hence the cup-to-disc ratios were higher in the GC group showing more damage to the optic nerves. Even though all the patients had comparable age, gender, and comorbidities, two of them had a family history of glaucoma which was in the GC group. These findings support the need for continuous assessment of the thickness of RNFL and GCC through OCT in the glaucoma patient population for signs of progression of the disease.

CONFLICT OF INTEREST

We declare that there was no conflict of interest.

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AUTHORS CONTRIBUTIONS

Topic selection:
Data collection:
Article writing:
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Proofreading:

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