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EFFECTIVENESS OF OPTICAL COHERENCE TOMOGRAPHY FINDINGS IN SPARING VARIOUS INVASIVE INVESTIGATIVE MODALITIES TO DIAGNOSE EARLY PAPILLOEDEMA

Ophthalmology

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ABSTRACT

Background : Papilloedema in early stages is very difficult to diagnose clinically. OCT findings effectively diagnose early papilloedema to institute management early to obtain better prognosis so much so to avoid life threatening situations. More or less undesirable effects and stress of invasive techniques may be avoided.

Objectives : The purpose of our study is to evaluate peripapillary retinal nerve fibre layer thickness, peripapillary total retinal thickness and subretinal hyporeflective space in papilloedema by OCT

Methods : We studied twelve diagnosed patients of mild and moderate papilloedema who attended the OPD of RIO and SRN hospital Detailed meticulous history was obtained from patients, their relatives or existing records. General and neurological examination, vision, refraction, BCVA, pupillary reactions (especially RAPD), direct and indirect ophthalmoscopy was performed. Retinal nerve fibre layer thickness, peripapillary total retinal thickness including subretinal hyporeflective space (SHYPS) was evaluated by OCT.

Results : Although average RNFL thickness was found to be higher in mild (171.70 ± 36.02) and moderate (183.14 ±8.14) papilloedema but average PTR thickness was found to be much higher and diagnostic even in mild (556.90 ± 11.69), what to say of moderate (718.28 ± 14.84) papilloedema.

Conclusion : Peripapillary total retinal thickness, shape and configuration of triangular SHYPS is more valuable as compared to RNFL thickness in diagnosing papilloedema in earlier stages.

KEYWORDS

Optical coherence tomography, peripapillary retinal nerve fibre layer thickness, peripapillary total retinal thickness, retinal venous occlusion, subretinal hyporeflective space (SHYPS).

Papilloedema is defined as swelling of the optic disc due to axoplasmic flow stasis in the optic nerve head. This clinical condition usually occurs following increased intracranial pressure. Clinically the condition may be suspected if patient complains of floaters and transient obscuration of vision, supplemented by features of increased intracranial pressure such as headache and vomiting. Papilloedema, if not diagnosed accurately in mild stage, may deny the benefits of various interventions and may even be life threatening. It is known to every ophthalmologist that in cases of subtle disc oedema and pseudopapilloedema, the importance of early diagnosis increases many folds, and any sort of diagnostic dilemma may prove dangerous.

Previous meticulous fundus examination and fluorescein angiography happens to be fundamental and important diagnostic tools for diagnosis of papilloedema. There might be difference in opinion regarding ophthalmoscopic evaluation of fundus findings in papilloedema. Fluorescein angiography on the other hand is an invasive technique, having toxicity due to dye along with other side effects.

It has been observed that the important clinical parameter to distinguish papilloedema from pseudopapilloedema is the swelling of peripapillary retinal nerve fibre layer. This retinal nerve fibre layer swelling usually obscures the retinal vessels as they cross the disc margin, whereas in pseudopapilloedema, this finding may not be evident. Apart from this there may be accumulation of subretinal fluid above retinal pigment epithelium in peripapillary region, which is demonstrable on OCT as a hyper-reflective space. This is specifically measured as peripapillary total retinal thickness (PTR). OCT is a non-invasive technique which permits high resolution cross sectional imaging of optic disc and surrounding retina , which may be utilized to diagnose and differentiate papilloedema from pseudopapilloedema.

Shashi Ahuja et Al (2015) did a study on 100 cases and 126 controls, performing OCT. They found a strong positive correlation between RNFL thickness and the Frisen scale for grading papilloedema. They recommended OCT as a routine non-invasive quantitative tool for detection of early papilloedema. A study done by Giacomo Savini et al in 2006 stated that RNFL oedema as detected by OCT may provide valuable information in optic disc oedema (ODE).

However, Karam EZ et al in 2005 and Sanchez-Tocino H et al in 2006 were of the opinion that RNFL thickness as observed by OCT may miss mild papilloedema. Later on in 2011, Vardanian Vartin C et al did a study on 24 patients and in 2010 Collin J Scott studied 36 patients and found that peripapillary total retinal thickness (PTR) may be a more sensitive and useful parameter for diagnosing early papilloedema.

There is no denying that papilloedema, especially if detected in earlier age group, requires urgent diagnostic and therapeutic interventions. Recently, many authors have worked with the opinion that OCT, a non-invasive technique, can detect and quantify diffuse thickening of peripapillary RNFL in eyes with papilloedema. Further, Vardanian Vartin C et al (2011) and Savini et al (2006) stated that PTR thickness with presence of subretinal hyporeflective space is more important to diagnose papilloedema, especially of mild grade.

The present study aims to evaluate peripapillary RNFL thickness, PTR thickness and SHYPS and to know whether their shape, thickness, configuration and other parameters may be helpful in diagnosing papilloedema, especially of mild grade, to avoid the undesirable effects, stress and financial burden of costly, extensive and invasive procedures.

MATERIALS and METHODS

The present study was undertaken upon patients attending OPD at

Regional Institute of Ophthalmology, M.D. Eye Hospital, Dr. Katju Road, Nakkhas Kona, Prayagraj and S.R.N. Hospital, Prayagraj, from July 2018 to November 2019. Permission was obtained from ethical committee, M.L.N. Medical College, Prayagraj. Written informed consent was taken from all patients

Patients having presence of clinical findings suggestive of mild to moderate grade of papilloedema were included in the study. Exculsion criteria were:

1. High ametropia (refractive error more than 6D of spherical and 3D of astigmatism)
2. Findings suggestive of any coexisting retinal or other optic nerve pathology
3. Chronic papilloedema and/or atrophic papilloedema
4. Intractable glaucoma
5. Compromised clarity of media

A detailed meticulous history was obtained from patients or their relatives. Age, sex, chief complaints and duration were enquired. Sometimes leading questions pertaining to disc oedema and increased intracranial pressure were also asked. If patient had been referred by neurology department, basic data regarding history and complaints as mentioned in records were noted. History of any previous investigations and treatment was also recorded.

General examination including neurological examination, with special emphasis on signs of increased intracranial pressure, was recorded. All related cranial nerves, presence of features of hemiparesis or hemiplegia were recorded.

Vision assessment was done on Snellen's chart in dark room. Refraction under full cycloplegia and Best Corrected Visual Acuity (BVCA) were recorded. Pupillary reaction, both direct and consensual and RAPD was noted. Focal anterior segment examination and anterior segment biomicroscopy was done by DC-3 Digital Slit Lamp Topcon. Direct and indirect ophthalmoscopy and +90D lens (Volk) was used in slit lamp for optic disc biomicroscopy in fully dilated pupil. If vision permitted field examination. Optical Coherence Tomography in fully dilated pupil by Cirrus HD-OCT (software version 5.0; Carl Zeiss Meditech, Inc) was performed for peripapillary RNFL thickness and peripapillary TR thickness as follows:

Peripapillary RNFL Thickness

Examination of patients diagnosed as mild to moderate papilloedema was done on high resolution OCT system. Scans were obtained by positioning it with 3.54mm circle centered on optic disc. In our OCT, rectangular scans of 6mm x 6mm cube were obtained. The measurement of RNFL thickness between its anterior border (internal limiting membrane) and posterior border (less reflective layer) was obtained. Overall average RNFL thickness alongwith RNFL thickness in inferior, superior, nasal and temporal quadrants were also obtained.

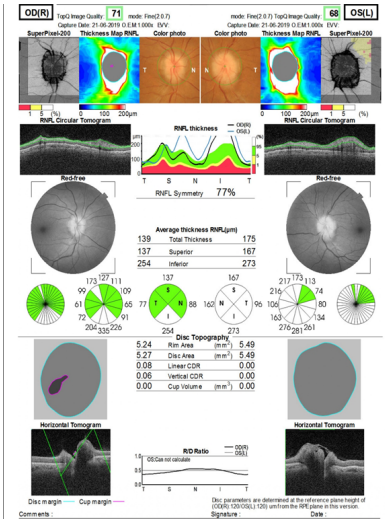


Fig.1 Showing RNFL thickness in papilloedema

Peripapillary Total Retinal (PTR) Thickness

The algorithm of this protocol is used to measure thickness of internal limiting membrane (ILM) and retinal pigment epithelium (RPE). This measurement usually exhibits total retinal thickness. This PTR thickness was evaluated in all the quadrants as temporal, superior, nasal and inferior. Our machine depicted thickness in various quadrants within different circle areas i.e. 1mm, 3mm and 6mm, but we measured PTR thickness within a circle area of 1-3mm. It has been observed that this 1-3mm area of PTR thickness measurement provided very much valuable and accurate information as compared to 3.4mm RNFL thickness circle area because in 1mm circle, RPE is absent and 6mm circle is too far from the disc. Multiple scans were obtained to get average parameter.

Subretinal Hyporeflective space (SHYPS)

This triangular space is located between sensory retina and RPE alongwith chorio-capillary complex. This space is known as Subretinal Hyporeflective Space. Alongwith this, the shape and configuration of SHYPS was also measured manually.

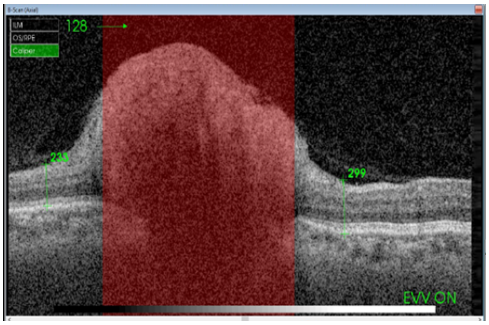


Fig.20.1 Showing subretinal hyporeflective space (SHYPS) thickness

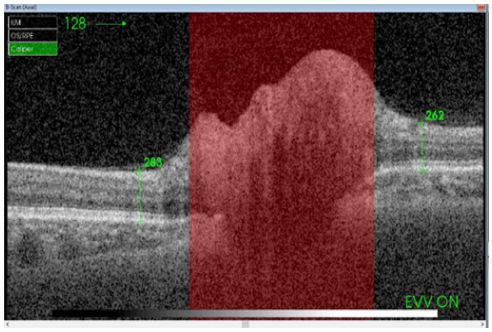


Fig.20.2 Showing subretinal hyporeflective space (SHYPS) thickness

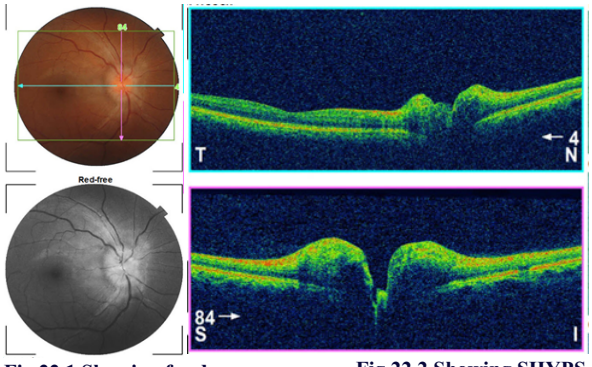


Fig.22.1 Showing fundus picture of papilloedema

Fig.22.2 Showing SHYPS in case of papilloedema

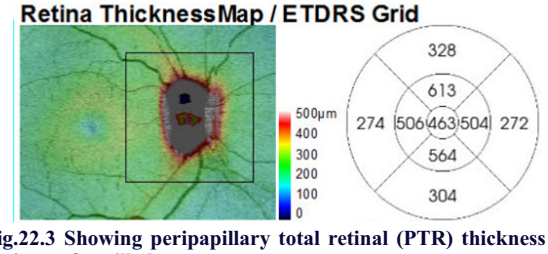


Fig.22.3 Showing peripapillary total retinal (PTR) thickness in patients of papilledema

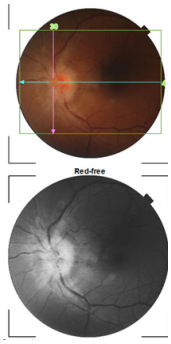


Fig.23.1 Showing fundus picture of papilloedema

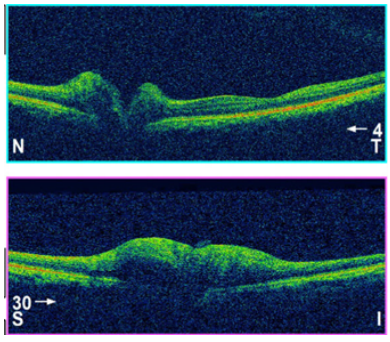


Fig.23.2 Showing SHYPS in case of papilloedema

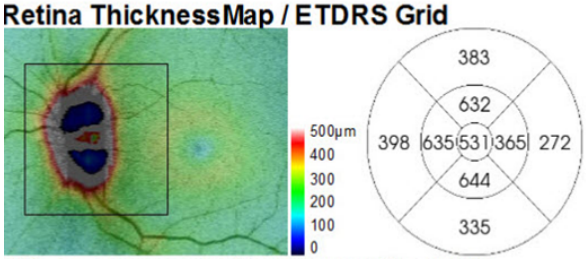


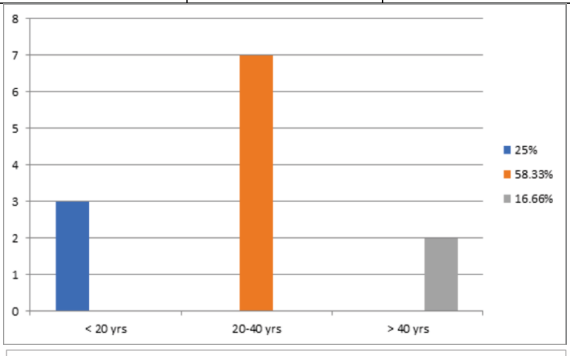
Fig.23.3 Showing peripapillary total retinal (PTR) thickness in patients of papilledema

OBSERVATIONS

This study with twelve patients of papilloedema was undertaken to study the peripapillary RNFL and peripapillary TR thickness imaging by Cirrus HD-OCT. The results were analysed using statistics calculators version 4.0 Analysis of Variance (ANOVA) and relationships are considered significant if p<0.0001

Table 1 – Age distribution of subjects under study

Age in years	Number of patients	Percentage
<20	3	25.0
20-40	7	58.33
>40	2	16.66
Total	12	100



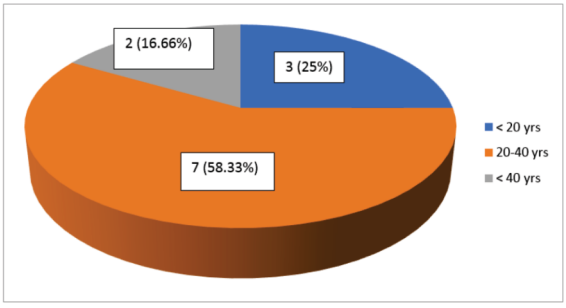
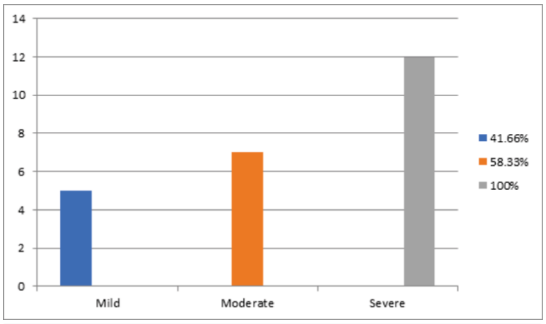


Table 2 – Grade of pailloedema in patients under study

Grade of papilloedema	Number of ptients	Percentage
Mild	5	41.66
Moderate	7	58.33
Total	12	100.00



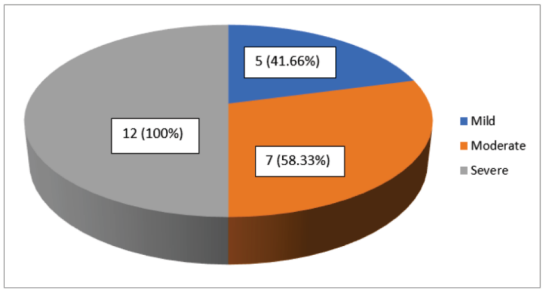


Table 3 – Showing peripapillary RNFL thickness parameters in cases of mild and moderate papilloedema in µm

Quadrants	Mild papilloedema	Moderate papilloedema	p-value
Average	171.60 ± 17.59	183 ± 8.14	0.158
Superior	259.70 ± 36.02	151.21 ± 14.39	<0.0001
Inferior	219.30 ± 30.94	263.30 ± 10.20	0.0017
Nasal	118.40 ± 25.72	124.85 ± 38.66	0.7532
Temporal	79.50 ± 12.90	85.30 ± 9.61	0.3869

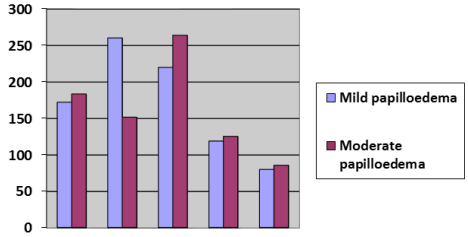
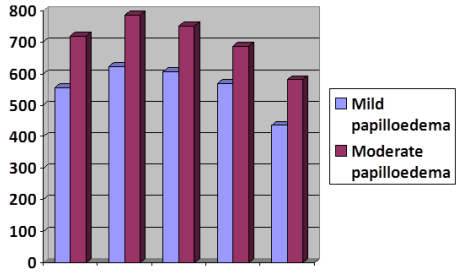


Table 4 – Showing total retinal thickness in mild and moderate papilloedema in µm

Quadrants	Mild pailloedema	Moderate papilloedema	p-value
Average	556.90 ± 11.69	719.28 ± 14.84	<0.0001
Superior	623.70 ± 10.32	786.00 ± 5.34	<0.0001
Inferior	607.40 ± 40.32	752. 78 ± 7.27	<0.0001
Nasal	570.20 ± 6.5	688.21 ± 5.47	0.0006
Temporal	436.80 ± 70.8	582.0 ± 10.01	0.0003



RESULTS

1. Maximum number of patients (7, 58.33%) were encountered in the age group of 20-40 years, which is definitely the younger age group. (Table 1)
2. Out of twelve patients subjected under investigations, randomly 7 (58.3%) were having moderate grade papilloedema. Five patients (41.6%) were having mild papilloedema. The grading was done on the basis of clinical and fundus examination. (Table 2)
3. Superior RNFL thickness exhibited a bit higher quantum of thickness (240.50 µm) in mild papilloedema, while inferior peripapillary RNFL thickness exhibited comparatively higher

quantum of thickness (263.00 µm) in moderate papilloedema. Mild and moderate papilloedema did not exhibit much difference in peripapillary RNFL thickness (Mild – 171.70 ± 36.02, moderate – 183.14 ± 8.14, p-value 0.1589). (Table 3)

4. A clear cut evidence of much higher quantum of average and mean PTR thickness was observed in both mild and moderate papilloedema. An increasing trend of average PTR thickness and mean PTR thickness was observed as grade of papilloedema increases. (Table 4)

DISCUSSION

It has already been documented that there is swelling of peripapillary RNFL in papilloedema. Thus clinico-imaging status of peripapillary RNFL may be one of the important diagnostic points in papilloedema. Clinically peripapillary RNFL status may be evaluated by ophthalmoscopy examination using red free light and NFL Photography. Apart from this, multicolor scanning laser imaging has also been employed (to measure the thickness of NFL to distinguish papilloedema) in which scans of retina using three different wavelengths of light (red, blue, green) are taken. OCT provides high resolution cross sectional visualization and direct measurements of NFL thickness. Low coherence light is employed through a non-contact, non-invasive instrument and depicts the retinal microstructure with a resolution of 10 µm. In the present study, we specifically evaluated the protocol measuring peripapillary RNFL thickness between its anterior border (internal limiting membrane) and its posterior border (which is obviously the less reflective border). We obtained a standard 3.4mm diameter circular scans centered on optic nerve head which is commonly used to measure peripapillary RNFL thickness.

The observations of our study revealed a remarkable thickening of peripapillary RNFL in true disc oedema due to axonal stasis. The average peripapillary RNFL thickness in mild and moderate papilloedema was found to be 171.60 ± 17.59 and 183 ± 8.14 respectively. We observed a statistically significant difference (P<0.0001) in peripapillary RNFL thickness in both mild and moderate papilloedema as compared to normal subjects (average peripapillary RNFL thickness in normal subjects). Thus obviously there should be no confusion to diagnose even mild papilloedema on the basis of peripapillary RNFL thickness. Similar observations were also recorded by Giacomo Savini et al by studying 9 patients with optic disc oedema (ODE) by evaluating that mean RNFL thickness which was statistically higher in patients with true disc oedema.

In another study done in 2005 on 13 patients of papilloedema and 13 controls, Marcel N. Menke et al observed statistically significant difference in average peripapillary RNFL thickness between papilloedema and normal subjects. But when we review the literature upon the subject, we find that this clear cut situation having no diagnostic dilemma does not prevail everytime.

Vardanian Vartin C et Al did a study in 24 eyes of 24 patients with papilloedema caused by increased intracranial pressure and observed that average RNFL thickness in mild papilloedema group was not significatly different than normal. Karam EZ et al in 2005 was also of the opinion that OCT RNFL thickness measurements may not provide a clear cut diagnostic clue and may even miss mild papilloedema. Gema Rebolleda et al in 2017 published a review article with the opinion that mild thickening of peripapillary RNFL is unhelpful as it is found in both early papilloedema and pseudopapilloedema.

Contrary to this, the quantum of thickness of peripapillary RNFL in our study as evaluated by OCT provides a better diagnostic clue for mild papilloedema. The higher quantum of peripapillary RNFL thickness (171.60 ± 17.59 µm) in our study is probably because patients might have presented in comparatively later stage of the disease, so much so that these cases might have been in a situation to enter in the stage of moderate papilloedema. This fact is also being potentiated by the observation that our study revealed statistically insignificant difference in RNFL thickness of mild papilloedema (171.60 ± 17.59 µm) and moderate papilloedema (183 ± 8.14 µm).

While evaluating quadrantic peripapillary RNFL, our study revealed highest quantum of thickness in inferior quadrant in both mild (219.30 ± 30.94 µm) and moderate (263.30 ± 10.20 µm) papilloedema. But on comparison, this difference in amount of thickness is statistically insignificant (p = 0.0017)

In our study, temporal quadrant exhibited least quantum of thickness in both mild and moderate papilloedema, followed by nasal, superior and then inferior. Surprisingly, superior quadrantic RNFL thickness in moderate papilloedema was found to be in extremely lesser quantum (151.21 ± 14.39 µm) and in comparison with mild papilloedema (259.70 ± 36.02 µm) the difference was found to be statistically significant (p value > 0.0001). In rest of the quadrants, the difference was found to be statistically insignificant.

In 2015, Shashi Ahuja et al performed a similar study to evaluate RNFL thickness in papilloedema and observed that RNFL thickness in inferior and superior peripapillary region was greater and is of higher grade in papilloedema. Contrary to this, Vardanian Vartin C et al did not observe any quadrant wise difference in RNFL thickness in any grade of papilloedema. Although in his study, average RNFL thickness was observed very carefully.

As regards in our study, average quadrant wise RNFL thickness did not exhibit much difference as mild (171.70 ± 36.09 µm), moderate (183.14 ± 8.14 µm) (p value = 0.1589) papilloedema. Some authors such as Menke MN et al, Karam EZ et al and Vardanian Vartin C et al had observed that average RNFL thickness as measured by OCT may miss mild papilloedema. We are also of the opinion that mild papilloedema in initial stages may not produce much difference as regards to quantum of RNFL thickness, but it is evident from our study that in later stages of mild papilloedema and before patient enters in moderate grade, we definitely can have an idea of diagnosis of papilloedema, eliminating normal and even pseudopapilloedema.

We also evaluated peripapillary total retinal thickness (PTR). The algorithm of PTR thickness protocol usually denotes the edges of internal limiting membrane (ILM) and retinal pigment epithelium (RPE), which shows total retinal thickness. Normally there is no leakage into the peripapillary subretinal space because of barrier property of intermediary tissue of Khunt. When this barrier of Khunt tissue is disrupted in certain circumstances, there is leakage into the peripapillary subretinal space, as observed by Samuels et al in cases of optic disc oedema (ODE). The significance of peripapillary total retinal thickness (PTR) in CRVO has also been emphasized by Menke MN et al. They observed a thicker peripapillary total retinal thickness (PTR) value in RVO. They were also of the opinion that diabetic oedema group have significant increase in PTR thickness.

PTR thickness in all four quadrants may be displayed in three circles as :

1. The innermost circle, diameter of 1mm
2. The middle circle, diameter of 3mm
3. The outermost circle, diameter of 6mm

Although peripapillary total retinal (PTR) thickness is displayed by our machine in all three circles, but we have taken cognizance of the thickness measurement in peripapillary circle area measuring 1-3mm. Vardanian Vartin C et Al in 2010 has also investigated circle area measuring 1-3mm. They excluded central 1mm area circle where RPE is usually missing. In their opinion the 3mm circle area provides better information as compared to 3.4mm circle area. Our study also revealed clear cut importance of PTR thickness. We observed substantial PTR thickness in mild papilloedema (556.90 ± 11.69 µm) and moderate papilloedema (718.28 ± 14.84 µm). It has been observed that the difference in average PTR thickness in mild papilloedema (556.90 ± 11.69 µm) and moderate papilloedema is statistically significant (P<0.001).

PTR thickness in our study is much greater in moderate papilloedema. This is indicative of the fact that as grade and severity of papilloedema increases, PTR thickness also shows higher grade of measurement. As PTR thickness is because of subretinal fluid accumulation in peripapillary area, it is logical also to believe that higher the grade and severity of papilloedema, greater is the PTR thickness and values. Due to this, even mild papilloedema has got quite substantial PTR thickness.

Regarding PTR thickness measurements, similar opinion has also been documented by Vardanian Vartin C et al in 2011. They studied 24 eyes of 24 patients of papilloedema caused by increased intracranial pressure and measurements of RNFL and PTR thickness were made. In their study, average PTR thickness was much greater in moderate and severe papilloedema in comparision with mild and control group. Similar observations have also been made by Giacomo Savini et al,

who have probably given the concept of PTR thickness for the first time. Moreover, average PTR thickness was much greater even in mild papilloedema group as compared to normal subjects. It clearly reveals that sensitivity of PTR thickness in mild papilloedema cannot be overemphasized. Thus our study also narrates that PTR thickness is more sensitive in diagnosing even mild papilloedema, what to say of moderate and severe papilloedema. Findings of our study are also coherent with many other studies that a stronger correlation between papilloedema grade and PTR thickness exists than RNFL thickness.

Proceeding further, Giacomo Savini et al first observed a triangular peripapillary hyporeflective space between internal sensory retina and RPE. They advocated the term subretinal hyporeflective space (SHYPS) and told that this space could be visualized by using linear scan crossing of ONH in cases of ODE with increased PTR thickness.

In continuation, observation of SHYPS has also been advocated by various other authors such as Ozge Sarac et al. They also told that in patients with ODE, the thickness of SHYPS is much increased. Lenworth N. Johnson et al also evaluated similar findings that the thickness of SHYPS is much greater in optic disc edema (ODE) as compared to optic nerve head drusen (ONHD).

Lenworth N. Johnson et al did a study by obtaining OCT images of 60 subjects (20 ODE, 20 ONHD and 20 controls). They observed cases both qualitatively and quantitatively. Qualitative features included elevated ONH with smooth internal contour and SHYPS with reconstrant-Lazy V pattern. Their study revealed qualitative comparison in RNFL thickness and SHYPS thickness.

Thus we are of the opinion that peripapillary total retinal thickness appears to be the most sensitive observation as compared to RNFL thickness measurement in diagnosis of papilloedema. Apart from this, PTR thickness measurement has emerged as the strongest observational tool to differentiate and diagnose mild papilloedema from normal subjects.

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